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One of the outstanding discoveries of modern science is that the human body is the home of multitudes of germs and parasites, some beneficent, some pernicious. The maintenance of health depends upon our knowledge of the nature and activities of these minute organisms, especially those which cause disease. In this volume many aspects of man's struggle for health are surveyed and a clear account is given of how these microscopic enemies enter the human body, how they disturb the balance of health, and how their action can be controlled.

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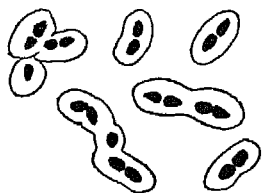
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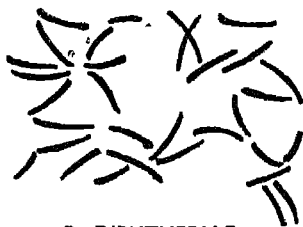
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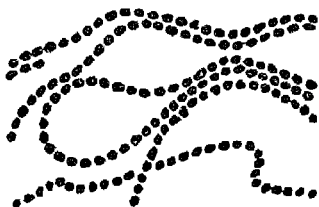
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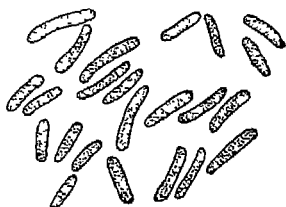
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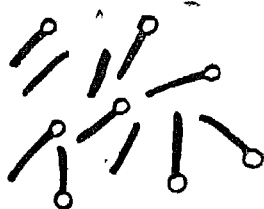
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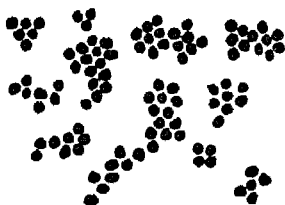
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BY

D. STARK MURRAY

B.Sc., M.B., Ch.B.

*Author of Your Body: How it is Built
and How it Works, etc.*

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THIS BOOK IS PRODUCED IN COMPLETE
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PREFACE

DISEASE is a subject on which mankind has taken a long time to acquire a rational outlook. To the individual stricken suddenly while in apparent health, disease can be a very terrifying thing. To the community those diseases which spread rapidly or attack a whole group simultaneously have an economic and psychological significance which has in the past led to an immense amount of speculation and theory both as to the cause of disease and as to the normal functioning of the human body. To-day we possess much knowledge on both, and for that knowledge the ordinary public is more than eager, although not always well served by those who try to give it to them. In this short book I have tried not only to give as much information as possible but to give it in language which will be readily understood. The translation of scientific language is not always easy, but I hope it has been achieved in these pages; I hope also that the drawings will assist in making the story clear.

D. S. M.

April, 1947

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CHAPTER I

THE PROBLEM

WHAT should be our attitude towards disease? Should we regard it as inevitable and to be accepted as something that mankind must always suffer? Should we take a morbid interest in it as many do, shuddering, but at the same time enjoying stories of all the horrible things that can happen to us? Or should we recognize that although the human body is liable to many different and often dangerous diseases, these must be studied, and ways found not only of treating them but of preventing them?

Disease and death probably play a greater part in the life both of the individual and of the community than any other of the problems with which mankind is concerned. Death, we recognize, is inevitable; yet man has always tried to find a way by which death can be defeated and has certainly attained considerable success in postponing that inevitability. The death from which none can escape should come at the end of a long and healthy life. This prospect is, however, always endangered by disease—that is to say, by departure from the normal healthy state—and this may be inherited or acquired. The greater number of diseases are, as we shall see, acquired, and many attack the body from outside. There are some that are trivial and cause only a temporary departure from normal, but a very large number are dangerous both to health and to life.

The problem with which we are still faced is that of reducing the virulence of all diseases, so that the life of the individual may be disturbed as little as possible. To a great extent the success that has been achieved in delaying death has resulted from the discovery that certain previously fatal diseases can be treated and prevented. The problem that now faces man is the final discovery of all the causes of disease as yet hidden, and the perfection of methods of preventing and treating the more serious of the death-dealing diseases.

There is no need to remind the reader that there has been a very large increase in the "expectation of life" during the past hundred years. We can anticipate a still further increase, which will be speeded up the more people understand how the search for health goes on and the part they can play in the battle against disease. This necessarily means that we shall deal here with the chief diseases and only with the principal causes of disease. It must not, however, be forgotten that many so-called minor ailments may be the beginning of very serious complaints and that this aspect of disease deserves a full share of attention. When the great classes of infectious, parasitic, and cancerous diseases have been finally conquered, there will still be a large amount of human suffering from comparatively small defects which at the present time are so often neglected.

It is not widely realized that many of these minor ailments may be of great diagnostic importance, pointing to the beginning of changes which may prove serious or even fatal. In this connection we shall later touch on the importance of rheumatism, so often completely neglected in its early stages, at

which, even with our present knowledge, something of lasting benefit might be done. The public have a responsibility in this matter, for most people disregard trivial illnesses and fail to take advice about them. In the new organization of the medical services which is taking place all over the world, this is one of the points on which a great advance can be made; co-operation between the lay public and the medical profession in discussing and analysing the trivial complaints will lead to a further advance in our knowledge of the way in which the human body can be maintained at a level of health as high as possible.

It is perhaps as well to clear up the question whether disease is a phenomenon only of civilized communities and whether it is likely to affect mankind more in the future than in the past. We have abundant evidence that a large number of diseases which we know to-day existed in past ages. It is true that we have removed many of the hazards, particularly the accidental, to which primitive man was subject, but we have added others caused by industry and environmental conditions with which primitive man was not troubled. A close study of history shows that in many instances disease has had an even greater effect on world history than all the intrigues of courts and all the bravery of soldiers. Indeed, there have been occasions when the intervention of a deadly epidemic disease, such as typhus, has changed the whole history of the world. It is probable that some of the great disasters that have occurred to certain highly developed civilizations, as revealed by the work of archaeologists, were due to the decimation of populations by disease. This is a danger not entirely removed from even the most

highly civilized races to-day and is certainly possible among those sections of mankind which are still comparatively primitive.

Those past epidemics gave rise to many superstitions and wrong theories about disease. Throughout all ages there has been opposition to the scientific study of the human body, and for a long time this delayed the discovery, not only of the normal functions of the various organs of the body, but of the causes of disease. It cannot, of course, be assumed that a knowledge of what is normal in a human body means that the individual will maintain his body in perfect health; but it is quite certain that complete ignorance of the elements of simple anatomy and physiology lays the individual open to all kinds of beliefs which may actually foster disease, or at least make him an easy victim for those charlatans who are always ready to exploit man's fear of death. One modern aspect of this is the existence of certain cults of healing which claim that all diseases are caused by one change in the human anatomy, or one habit of human beings, and hence that all diseases can be prevented or cured by one simple device.

Scientific medicine has shown that this idea of a single cause for all disease will not bear even the most superficial investigation. The human body is composed of uncountable millions of cells, varying in size, shape, and relation to each other, varying even in fundamental chemical construction and very widely in function. A derangement of functions in any of these may cause changes, amounting to disease, in the body as a whole. In addition, however, it has been shown that this combination of diverse units which we call the human body is subject to many outside

influences. It gives almost innumerable responses to these influences and is attacked by a great variety of bacterial and parasitic enemies.

Broadly speaking, the causes of disease are not very numerous and can be classified in certain large groups, according to their nature or according to the effects they have on the human body. Within each group, however, there are almost endless numbers of agents, each of which produces a condition of the body which is so definite as to be clearly recognizable as a separate entity in spite of the general character of the group to which it belongs. When we consider that most of these agents may attack each of the separate organs of the body, or the body as a whole, and that the changes in the organs are not always the same, we find that the causes of death from disease run into many hundreds.

It cannot, therefore, be too strongly emphasized that if the world of the future is to be rendered free from the more dangerous diseases, dependence must be placed on what is called orthodox medical science rather than on the unscientific theories of disease which are always being brought forward. There are still many gaps in our scientific knowledge, but the methods by which we check and increase that knowledge are those common to all scientific methods and must be pursued in a rational manner. It is probably true that many of the exponents of medical science are not sufficiently well grounded in it to be efficient in the fight against disease, and that many work under conditions which do not enable them either to make use of the knowledge they already possess or to keep pace with all modern developments. The organization of the medical profession is far below optimum

efficiency, because the work is unsystematic and the arrangements permit at one and the same time much overlap and many gaps.

It is also worth remembering that the knowledge embodied in medical science has not been gained by a definite, co-ordinated plan; it has resulted from the work of innumerable and very often forgotten workers. In the past it has received very little encouragement and help from the community or the State. Scientists have had to struggle along with incomplete apparatus and equipment, begging for help which "in the past has been given grudgingly as a luxury which the community could ill afford." Lacking the resources which would enable them to carry out their researches with full efficiency, the scientists deserve all the more credit for having discovered so many of the fundamental causes of different diseases and devising methods by which they can be successfully treated or completely prevented. It is with a description of these discoveries that we are concerned in the following chapters. By showing something of what has been achieved we hope to be in a position, at the end of the book, to consider what further advances can be made.

CHAPTER II

THE DISCOVERY OF GERMS

MAN'S imagination has at all times filled the air with a great variety of invisible creatures—fairies, goblins, spirits, and ghosts—and as knowledge developed he began to speculate on the possibility that there were other invisible creatures who played a real part in his life. To-day we know that that speculation was correct; in fact that all around us—in the air, the water, the dust, on our bodies, clothes, and furniture—are millions of minute living creatures whose existence has been proven only in comparatively recent times.

These living creatures have been given many names—bacteria, microbes, germs, or organisms—and their discovery was made possible only by the invention and perfection of the microscope, giving a magnifying power of many hundreds of times. The first man who saw microbes clearly and who recognized that they were living creatures was a Dutch investigator, Leeuwenhoek, who made his own magnifying glasses by a method which is still not clearly understood. In 1675 he described to the Royal Society in London the appearance of different germs. We may say that the science of bacteriology began in 1675 with his first announcement of the discovery of these "little animals," as he called them, but nearly 200 years went past before the first clear evidence was obtained that these minute creatures played an important part

in the life of man. Pasteur, the great French bacteriologist, was the first to realize that these microscopic organisms were capable of causing disease. His earliest study had nothing to do with human disease, for Pasteur was really a chemist and had been asked to investigate causes of putrefaction in certain wines. This led him to study the process of so-called "spontaneous generation," under which living matter was alleged to arise from dead matter. Pasteur showed, as indeed other investigators had shown earlier without their experiments being widely accepted, that there existed invisible germs capable of growth under certain favourable conditions, easily killed by such a process as boiling, but always present in the air. He demonstrated, in fact, that germs could arise only from germs that had existed before, and he realized that in this process they used up foodstuffs just as all living matter did. It was only at a later date that Pasteur saw the link between these germs and the diseases of animals and man. Before we go on to that subject we must therefore learn something of the fundamental characteristics of germs and the manner of their discovery.

All living matter is composed of a highly complex substance called protoplasm. In animals and plants this protoplasm exists in tiny packets which we call cells. The smallest conceivable unit of life is a single cell, and of all single-cell creatures bacteria are the smallest and simplest. Their very size indicates a complexity that is almost beyond imagination, for within their tiny bodies goes on every process necessary to existence. In order to see these creatures we must use a compound microscope which, by a combination of different lenses, gives us a magnification

of some hundreds of times. The magnification commonly used is about 1,000 times, which enables most of the common germs, measuring something under 1/5,000th of an inch, to be seen easily. So small are most microbes that in order to describe them a special unit of measurement is used: the micron or μ (Greek "m"), which is 0.001 mm., or 1/25,000th of an inch. It is difficult to grasp what this means, but something of its significance is indicated by the calculation that if an organism 1μ long were magnified to look like one inch, then an inch magnified to the same scale would be 700 yards long. The smallest germs are about 0.25μ in length, while many are 3 to 5μ long, though much greater lengths may be reached.

The microscope with which we examine these small creatures is, of course, a remarkable instrument, which has been slowly improved over a long number of years. Leeuwenhoek used a single lens of great magnifying power, but in the modern microscope a number of lenses are combined. To allow as much light as possible to come through, and to give the highest possible magnification, these lenses have to be very carefully chosen, carefully ground, and combined. In recent years new inventions have gone far beyond even the finest compound microscope. The electron microscope, using an entirely different principle, now enables us to photograph germs at magnifications which are almost as much beyond comprehension as is the minute size of the germs they photograph. For ordinary purposes, however, the compound microscopes, in which most of the problems have been met by the makers, enable us to see the germs clearly and accurately.

The earliest investigators, such as Leeuwenhoek (1675), Joblot (1711), Spallanzani (1750), and many others, had to work with instruments which lacked the precision of those of the present day. They laid the foundation of all modern bacteriology when they tackled the question of where the germs came from, how they lived, and how they multiplied. They discovered that germs, like all other living matter, require moisture, a certain temperature, and certain food-stuffs, and that given these they could multiply at an astonishing rate. They showed that germs could be killed by boiling and that they could arise only from previously existing germs.

The experiments which Pasteur carried out on this point were conclusive and very neat. It was known that if a liquid, such as a solution of sugar or beetroot juice or an infusion of vegetables, was exposed to the air, it would decompose and germs appear in it. Pasteur made some narrow vertical flasks and partly filled them with such a fluid. He then heated the glass and drew out the neck into a series of curves. He next boiled the flasks until steam came out of the curved necks; when such a flask was left standing the fluid did not decompose and did not grow any germs. Although ordinary air could move in and out of the flask, the curves in the neck prevented germs from entering because these germs, being solid particles, collected in the narrower curved parts of the glass.

To-day we know that we can prepare fluids containing everything that is necessary for bacterial life and yet keep them uncontaminated for ever. This we do by various methods of sterilization, most commonly by heating (in the same way as the familiar

canning or bottling of fruit), though other methods are possible. If, however, even a single germ or its spore is left alive in such a fluid, or is allowed to enter it, microbic growth will at once begin. The rate at which this growth proceeds is more than astonishing. Many of the commoner organisms grow so rapidly that they become, in the mass, clearly visible in twenty-four hours. Thus a bacillus such as the *Bacillus Coli* will divide into two bacilli in about twenty minutes; each of these new organisms will at once begin to grow, and in twenty minutes division will again take place. That means that under ideal conditions a single bacillus would in eight hours produce 16,000,000 descendants. The weight of a single organism is infinitesimal, but in twenty-four hours it would, if allowed complete growth, produce about 500 tons of bacilli.

It follows from this that, if ideal conditions for bacteria existed everywhere, the world would be swamped by bacterial growth. There are, however, many factors which operate against such a possibility. Only the commoner organisms grow at the rate mentioned; others require days or even weeks to produce any appreciable weight of material. All of them require abundant foodstuffs and are subject to a large number of hostile substances which retard their growth or lead to their destruction.

Early bacteriologists did not get much beyond observing that germs actually existed and could be grown in fermentable fluids. Very many facts had been collected about them before Pasteur suggested that they might have a connection with human disease. He was, in the first instance, concerned with the part they played in the production of alcohol, but he was

soon led into investigating the part they played in the life of men. That they enter into many living processes and mechanisms of value to man we now know, but for our present purpose the important fact is that these tiny globules of protoplasm are capable of causing disease and death in the higher animals.

CHAPTER III

THE GROWTH AND IDENTIFICATION OF BACTERIA

THERE are almost innumerable methods available for examining bacteria, and a large number of tests have been devised by which the various germs can be accurately identified. This is important when we come to consider the treatment of diseases due to bacteria, for correct identification of the bacteria concerned often influences the treatment to be followed. Germs may, of course, be examined directly with the microscope, but more information is obtained if we are able to grow or cultivate the particular microbe under examination. To do this we must provide them with those foodstuffs which are essential for their growth. All bacteria require for their culture carbohydrates, a source of nitrogen, and certain salts; given these, most of them are quite easily grown.

The material which bacteriologists use is known as a culture medium, and the most common is a broth prepared from heart muscle soaked in water, to which may be added peptone and some common salt. Some broths are prepared by more elaborate methods which extract more substances from the muscle fibre than the simple method suggested. Others use prepared meat extract. Such combinations give a liquid in which most organisms will grow. Fluid media are, however, not always suitable. To obtain solid

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media, gelatine may be added to the broth, giving a solid mixture at ordinary temperatures. Germs usually grow best at body temperature (37.5° C.), at which gelatine is liquid, so this mixture is not always suitable. In its place is used a substance called "agar," prepared from a kind of seaweed found mainly in the Chinese seas. This produces a medium which is solid at incubator temperature; broth so solidified is the most common culture medium in use.

It is generally kept in glass test-tubes or bottles in the form of "slopes," made by allowing the agar to solidify while the tube is lying on its side. Formerly such tubes were closed by plugs of cotton wool, but to-day the most common form is a small bottle with a screw-cap and an inner lining of rubber or other substance to make sure that the stopper is air-tight. These tubes, after being filled with agar, are sterilized by heat, so that no live germs are present.

Sterilization in this case is usually effected by steam in either a Koch's sterilizer, which provides a temperature of 100° C., or in an autoclave, where, in addition to the heat, pressure is also used. Steam heat is used instead of dry heat, to avoid damage to the medium from evaporation of its contained water. The medium must be left in the sterilizer long enough to kill off all the ordinary germs. If there is any possibility that spores are present, the process must be repeated on three successive days; during the period between the successive sterilizations any spores present are certain to have germinated and changed to forms susceptible to heat.

When we want to grow some germs we inoculate or "plant" such a sterilized slope-tube with the matter thought to contain the bacteria. This matter may be

pus, sputum, or other material from a sick person. The planting is done by means of a bacteriological needle, usually called a "loop," which is a piece of fine platinum wire about two inches long, mounted in a metal or glass holder. The end of the wire is bent into a closed loop (Fig. 1). Platinum is gener-

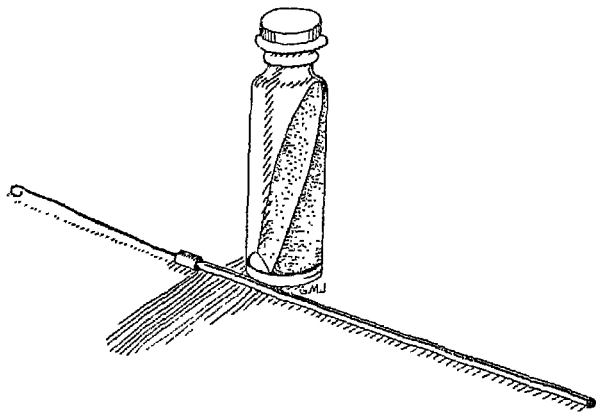


FIG. 1.—Solid culture media are usually kept in screw-top bottles and sloped so as to give a large surface for the growth of bacteria. The germs are spread with the platinum loop.

ally used because of its comparative indestructibility, but more particularly because it is very easily heated to red heat. If placed in an open flame, such as a Bunsen gas-burner, such a wire becomes instantly red-hot and is therefore completely sterilized, for no germs can resist that temperature. If we put the loop into a fluid containing germs, it picks up some of the fluid, which can then be transferred to a culture medium. We take out the cotton-wool plug or

remove the cap, and pass the mouth of the tube through the flame, so that no germs may drop in from the edge of the glass; then, holding the tube at an angle, so that air-borne germs cannot enter, we insert the platinum loop and rub it very gently over the surface of the culture medium, thus depositing the fluid containing germs which we had taken up in the loop. We re-seal the tube and place it in an incubator, which is maintained constantly at a temperature of 37.5°C .

When we inoculate a tube in this manner we may have deposited many organisms on the surface, but there will be nothing to see; except for the scratching caused by the loop, the medium remains clear. Twenty-four hours later, however, we find a change. Wherever an invisible organism was placed there has arisen a small mass visible to the naked eye; such a mass is a "colony," and each has developed from a single organism. These colonies increase in size for some time but become stationary when all the available foodstuffs around them have been used or when poisons, produced by the germs themselves, become too powerful. When this poisoning process occurs, the organisms will die unless conditions are changed.

We can now take the platinum loop again and, touching one of these colonies with it, transfer the bacteria to another tube of medium, thus making what we call a sub-culture. In this the germs go on growing again and produce new colonies. By repeated sub-cultures we can determine the behaviour of any germ under different conditions, and it is on such behaviour that organisms are classified. Nature has, fortunately, been kind to us in giving many germs characteristics so distinctive that bacteriologists

can recognize them easily. Some germs are, however, so closely related to others that more elaborate tests are required to identify them.

The characteristic most easily noted by the inexperienced is the colour of the germ, or rather of the colony. The most common colonies are white, but some are transparent or translucent; others produce yellow, golden, red, violet, or green pigment. Thus the *Staphylococcus Aureus* produces colonies with a beautiful old-gold tint (hence the name aureus). This germ causes a variety of diseases, of which the most common is the ordinary boil. It has, however, a "cousin" that is almost always harmless, the *Staphylococcus Albus*, which produces a pure white colony.

In most of the coloured germs the pigment produced remains in the body of the bacteria, but in some cases it passes out into the surrounding media. Thus the *Bacillus Pyocyaneus* produces rapidly, and in large quantities, a bright green pigment which at once penetrates the medium on which the bacillus is grown.

The next thing to be noticed about colonies of bacteria is their size; we may also note the rate at which the colonies grow. The staphylococcus mentioned above produces colonies $\frac{1}{8}$ th of an inch in diameter, but the streptococcus, a germ usually dangerous to man, seldom gives a colony larger than $\frac{1}{16}$ th of an inch. Colonies also vary in appearance, being smooth, shiny, wrinkled, dry, or tending to spread outwards, according to the class of organisms. Some germs are very motile and will cover the whole surface of the culture medium.

In considering the rate of growth of bacteria it is as well to note that many of them are particular about

their food and will not grow at their maximum rate unless the medium contains what they want. The plain agar-broth medium is suitable for some of the commoner germs, which on this medium give a heavy growth in twenty-four hours; others will grow only if blood is added to such a medium. Thus the germ called *Bacillus Influenzae*, because at one time it was thought to be the cause of influenza, requires the presence of blood in any medium on which it is growing. The bacillus which causes tuberculosis is even more difficult to satisfy, and is usually grown on a mixture of egg and glycerine, although even on that it takes many weeks to produce colonies of appreciable size.

Another way in which we can classify bacteria is according to whether they are "aerobes," which must have oxygen, or "anaerobes," which grow only if all oxygen is excluded. Special apparatus is used to ensure the absence of oxygen, this gas being replaced usually by nitrogen or hydrogen. There are a few bacteria which can exist either with or without oxygen, and there are some which grow better in an atmosphere which contains some oxygen, but not the normal amount. One or two like other conditions, such as an excess of carbon dioxide. There is also the interesting group of bacteria which can use and "fix" in their own bodies the nitrogen found in the air.

Apart from whether germs will grow in the presence or absence of certain substances, there is also the question of how they deal with the substances they do utilize. One of the first bacterial phenomena to be investigated was that of fermentaton, in which a carbohydrate, or sugar, is broken down with the

liberation of gas and the formation of other chemical products. All bacteria do not use the same carbohydrates in the same way. By cultivating pure strains of germs in a number of different "sugars"—as they are usually referred to in the laboratory—and noting which are fermented, it is possible to divide into separate families a large group of very similar bacilli, including those of typhoid fever and dysentery.

Temperature is another factor affecting bacteria. For the most part the organisms associated with man grow best at body temperature (37.5°C.). If they are frozen, they are almost completely prevented from growing. Freezing does not necessarily cause death, and even intense cold may be resisted, but at such low temperature the germs do not reproduce. Conversely, some germs are adversely affected by temperatures higher than blood heat; above 45°C. few continue to grow. There are, however, a few germs—the thermophylic bacteria—which grow in manure and in hot springs where the temperature is 55°C. or higher.

Then there is the faculty of some germs to affect others adversely—a faculty which has given rise to the discovery of Penicillin. Penicillin is derived from a mould, *Penicillium*, which was noticed by Sir Alexander Fleming to arrest the growth of certain other germs and indeed destroy some that had already developed. This is not a property of this particular mould only, since many others display it, and although the property is not of much value in identification, it is one of intense interest in the science of bacteriology.

So far we have mentioned only those characteristics which relate to bacteria "in the mass." When we

come down to individuals, there are other possible sub-divisions and other distinguishing features. In order to see germs under the microscope properly and to study them in detail, it is necessary to stain them. They are, in themselves, practically colourless, but when they have been killed by drying they readily take up certain dyes and so are rendered visible. Some common colours, such as methylene-blue, stain practically all bacteria and are therefore capable of showing the size and shape of germs. But it is fortunate that, even in their reactions to dyes, bacteria vary, and by using something more than a simple stain further distinguishing factors appear. The method of staining generally used, and one which is essential to the identification of all organisms, is that discovered in 1884 by Gram, a Danish bacteriologist. It requires the use of two dyes, one a solution of crystal violet and the other a contrasting red stain, such as basic fuchsin. Germs stained by this method, if they stain at all, either take up and retain the violet, and are therefore called "Gram positive," or, being unable to retain the violet, stain red and are called "Gram negative."

To stain bacteria in this way the usual procedure is to prepare them by placing the material containing them on a glass slide, which usually measures three inches by one. With a platinum loop some of the bacteria are spread out thinly on the surface of the glass (using a little water, if necessary) and allowed to dry in the air; the slide is quickly passed through a flame to dry the germs completely and cause them to adhere to the glass; the staining is then carried out. When the staining is completed the film is again dried and is ready for examination.

The high magnification usually employed requires a special lens, known as an oil-immersion objective, which gives clear definition of even the smallest germ if a drop of a substance such as cedar-wood oil is placed between it and the slide to prevent loss of light between the film and the minute lens of the objective. With such a lens it is possible at once to distinguish the Gram-positive and Gram-negative germs and to see their size and shape. The Gram stain is suitable for most organisms, but, as we shall see later, some, notably the tubercle bacillus, require a special method of staining.

There are further methods of identification, depending on the reactions of the human body to certain germs. We may also require to distinguish between such organisms according to their effects on other animals. Some have a selective action more dangerous to one animal than to another. There is also the fact that within the group injurious to mankind there are some which are themselves poisonous, and some which produce one or more poisons that pass out of their bodies and affect the body of man adversely.

So we see that, although Nature has made life more difficult for man by the disease-producing germ, she has also provided clues whereby they can be recognized. Their recognition and identification has already been followed by a satisfactory solution to the problem of cure, and even of prevention, of the microbic diseases.

CHAPTER IV

THE GERM THEORY OF DISEASE

IN the previous chapter we have occasionally taken it for granted that germs cause disease. This fact, however, is one that has been accepted only in comparatively recent times. The very early bacteriologist did no more than observe microbes, and it was not until about 1870 that definite evidence was obtained that germs actually cause disease. The idea in various speculative forms had occurred to medical men at earlier dates, but it was only with improvements in the microscope and other technical methods that proof was obtained.

To no one person can the full credit for this momentous discovery be given, but Lister in this country was probably the first to realize its importance to man. The story has often been told of his desire to improve surgical technique and of his keen interest in the work of Pasteur. He elaborated his own technique for "antiseptic" operations before evidence had accumulated to show how right he was in trying to exclude germs from surgical wounds. In Germany E. Klebs, who was later to establish the cause of diphtheria, came near to proving the theory, but it was Robert Koch who finally settled the point. His earliest work was published in 1878, and he was the first bacteriologist to realize and to demonstrate that a certain disease is always caused by one and the same organism. Koch's work, as will be emphasized later,

is still the foundation of many routine practices in a bacteriological laboratory, but his proofs that a microbe of one kind or another is frequently the cause of disease was a scientific discovery of enormous importance.

Many people find it difficult to believe that bacteria are almost universally present on and in natural objects. From this fact it follows that, if we make cultures from any parts of human bodies or of clothing, furniture, the soil, the air, and so on, we shall obtain a growth of organisms. It is therefore necessary as a first step, in identifying germs and in proving their relationship with disease, to make a "pure" culture of organisms, i.e. to make a culture from a single germ so that all the germs in it and in sub-cultivation will be true to type. The methods used to-day are many, but the most common is a variation of one devised by Koch in which, with a platinum loop, some germs are spread out on a large surface or plate of medium, so that single organisms become separated from their fellows. After a night in the incubator each of these gives rise to a colony from which a pure culture can be made. If any culture obtained by this method shows more than one type of colony, then all the types must be further tested (Fig. 2).

When we have isolated a germ in this way, we must devise methods of testing its connection with disease, and these methods must give us a definite answer. It has long been accepted that, before we can say that disease is caused by a particular germ, three conditions must be fulfilled. These conditions, usually known as Koch's postulates, "demand" that before a germ can be said to cause a disease it must
"(a) be constantly found in the diseased parts of the

body ; (b) *be capable of growing outside the body ; and* (c) *be capable of reproducing the disease if introduced into the bodies of animals or man.*" A further proof may be given if we can show that in the course of recovery from disease the body produces in the blood stream a substance or substances having a harmful effect on the germs under suspicion. The most complete form of proof is obtained when it is possible to

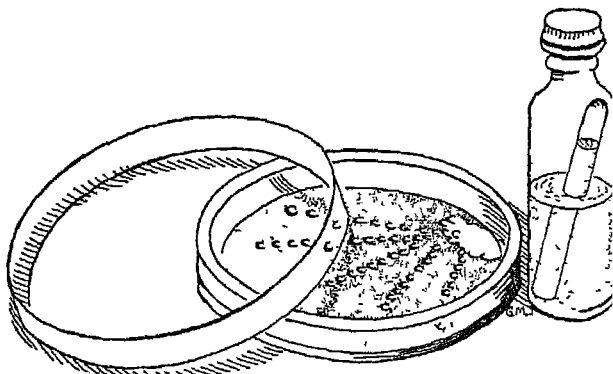


FIG. 2.—Germs may be spread on the surface of a plate of culture media. Others are grown in liquid medium containing a small tube to show the formation of gas.

take the blood thus shown to contain something antagonistic to the germ and to use it in the treatment of cases of the disease.

Let us take it for granted that germs do cause disease in the human body, and let us consider what happens. It is first of all necessary for the germs to gain entrance into the tissues. To do this, they may have to pass from one person to another ; therefore they must be capable of existing for some time outside the body. For most of them this is possible, although

their vitality varies considerably. Many germs, unless they are completely dry, or treated with heat or antiseptics, can live for a very long time in a state of "suspended animation." In other cases spores, which are, as it were, seeds from which a new germ can arise, are produced in large numbers, and these spores are very resistant to bad conditions. Some germs are, of course, carried by various agents from one person to another, and in fact most of them manage to enter the body in one way or another. This may be through the skin itself, although the skin is remarkably resistant to the entrance of germs; in most cases it is only when there is a cut, scratch, or abrasion that microbes are able to get through. Many organisms enter by a more vulnerable route, the respiratory tract—the nose, throat, the windpipe, and the lungs—in every part of which the warm, moist conditions are favourable to the growth of bacteria. There is also the digestive tract, where certain germs normally live in very large numbers, but where dangerous germs, such as the bacillus causing typhoid fever, may invade. Finally there is the genito-urinary tract, by which the organisms of the venereal diseases usually enter.

When germs gain entry into the body, Nature has provided certain defences, one of the most important being certain white cells in the blood stream, the "polymorphonuclear cells," which are described later in this book. It is these white cells that form pus, which is a mixture of them and the germs they are trying to resist. In pus we have a most convenient starting-place for a study of germs as the cause of disease. The proof of the germ theory of disease is, as will be seen, so remarkably simple and has been

confirmed so many times by so many observers that it is somewhat astonishing that many people still attempt to deny its validity.

The most straightforward example of pus-formation, and one of the simplest, is the common boil,

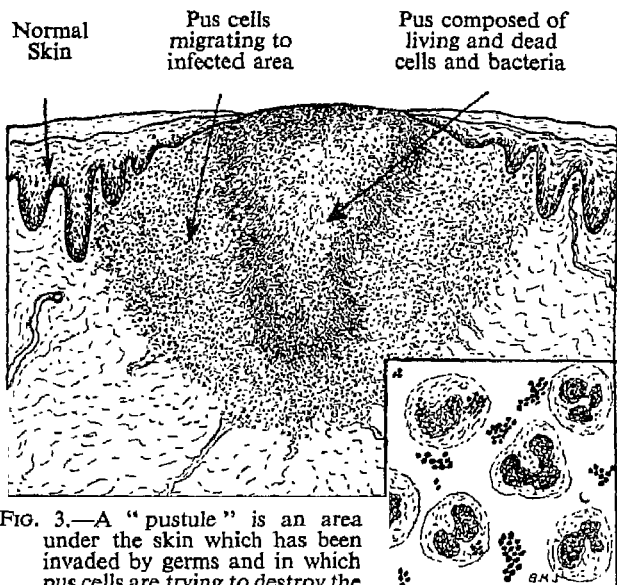


FIG. 3.—A "pustule" is an area under the skin which has been invaded by germs and in which pus cells are trying to destroy the invader. *Inset*: Pus cells and cocci.

which was one of the earliest studied by a bacteriologist. His name was Dr. Ogston, of Aberdeen Infirmary, and he made experiments on himself to demonstrate the effect of the germs in the pus from a boil. The boil is a small area of the skin in which there has been inflammation and in which pus has

been formed; the collection of pus under the skin causes the familiar swelling (Fig. 3). If we prick such a boil with a needle, the pus will escape; we can then take up some with a platinum loop and smear it on a glass slide. If we use the method of Gram-staining already described and put the glass slide under the microscope, we discover enormous numbers of pus cells, and among them little groups of darkly stained dots, spheres of about $1/25,000$ th of an inch in diameter. From the kind of groups they form, which are quite characteristic, they are called staphylococci—from the Greek word meaning grapes. We can stain films of pus over and over again by many different methods, and we shall always find that these same germs are present.

We now have to grow them outside the human body. We sterilize a platinum loop by heat, as already described, and, when it is cool, take up a small quantity of the pus and smear it over the surface of a tube of ordinary agar. This is incubated overnight, and next day the surface is seen to be studded with small round spots, the largest about $1/8$ th of an inch in diameter. These are the colonies of staphylococci, and they all show a rich golden-yellow colour, which proves them to be the pathogenic (disease-causing) *Staphylococcus Aureus*. The culture will almost certainly be "pure"—that is to say, containing no other germs—but if there is any doubt on this point we can transfer a single colony to another tube of agar, and in twenty-four hours we shall have a heavy growth of the organisms. We have now shown that the germ is constantly present in the pus, and we have grown them outside the body.

To complete the evidence it is necessary to repro-

duce the disease. Every patient who suffers from boils is apt to do it in the same way as we can do it experimentally. A few of the living germs are injected or rubbed into the scratched skin of a healthy person. This was how Dr. Ogston first tried out the germ theory. When the germs get through the skin, an abscess will be formed exactly like the original boil, and from this point we can go through the whole process of identification, growth, and test of the staphylococcus.

It must, of course, be clearly understood that not all diseases are caused by germs. There are defects of the body, to which we will refer later, that have nothing to do with the invasion of the body by an outside agency. But all those diseases known as "infections" are due to minute forms of life of one kind and another which find in the human body an ideal place to grow.

It is not always easy to obtain all the proofs that we require of bacterial diseases, for there are some germs so small that our ordinary methods of dyeing them and viewing them under the microscope may not reveal them. Recent developments, such as the electron microscope, in which enormous magnifications can be obtained by a new technique, may get over this difficulty in time. There are other germs which, while they grow freely inside the human body, prove very difficult to cultivate artificially. In a modern laboratory we use a large number of artificial culture media, composed of many substances known to be utilizable by germs; but there are a few germs which require conditions very delicately adjusted, and there are still some which, though easily seen and recognized under the microscope, cannot be cultured

without the greatest difficulty. For them we seem unable to provide exactly the conditions which they find in the human body.

There are also certain diseases in which the third part of the proof of the relationship to disease may be particularly difficult. Some diseases are too dangerous to be tested out on man himself, while others do not seem to have any effect on the small animals generally used for this kind of research. A very good example is the case of influenza, which baffled research workers until the ferret, an animal not usually used in the laboratory, was tested and found to be just as susceptible to this particular disease as mankind. In cases where the animal test is impossible, because we know of no animal that will take the disease, we may have to reach a conclusion and proof by indirect methods. One such method is the production, by the body itself, of substances harmful to the germ under examination.

One of the most serious of diseases definitely connected with a specific organism, and one of the first on which Koch worked, is tuberculosis. Many factors enter into the infection of a particular individual with this disease, but the fundamental cause is the tubercle bacillus. This is found in the diseased parts of the body; it can be grown outside the body; and when injected into a susceptible animal, such as the guinea-pig, it causes the typical disease. In this case, however, special methods have to be used, because the tubercle bacillus cannot be cultivated as easily as the staphylococcus described above. Staining by ordinary methods is extremely difficult, owing apparently to a surface coating of some fatty substance. On the other hand, once the tubercle bacillus

has taken up a dye it retains it, even if placed in acid or alcohol, which would remove the dye from most germs. This fact has provided us with a relatively simple method of identification, for in films containing more than one kind of germ—which is the usual case with sputum from cases of disease of the lungs—the tubercle bacilli stand out from all the other germs.

Tubercle bacilli are different from most other germs in their rate of growth. In the case of the staphylococcus the colonies are clearly visible in a few hours; the tubercle bacillus takes many days to show any appreciable growth. The staphylococcus and many others require only a relatively simple medium; the tubercle bacillus requires foodstuff of a very special kind. On the other hand, the third test—the proof that tubercle bacilli cause disease—is easy, for many animals are very susceptible to tuberculosis. This feature has been of considerable value to the human race, since it has enabled medical men to make an easy diagnosis of the disease in some cases. On the other hand, the fact that animals, and particularly domestic cattle, also suffer from tuberculosis has been one of the reasons why the disease has spread to so many human beings.

If any material containing tubercle bacilli is injected into the guinea-pig, the animal will become diseased in a short time, even though the number of bacilli was so small as to escape detection under the microscope. Strict precautions are, of course, taken against the animal suffering any pain, and such an experiment, apart from the proof it gives that tubercle bacilli are the cause of tuberculosis, may enable treatment for human beings to be developed with some prospect of success.

The organisms so far mentioned invade the body straight through the tissues and cause disease and death by, as it were, their personal presence in the body. This is not, however, the only way in which germs cause disease. There are some which do not cause damage by their actual presence in the tissues, but because they produce a poison, or "toxin" as it is called, which leaves the body of the germs and, entering the blood stream, is conveyed to all the tissues. The disease that ensues is then due to the action of this toxin. The most familiar case is probably diphtheria, in which the organism grows in one part of the body, usually the throat, where it causes a comparatively small local disturbance. Its poison, however, which rapidly passes to all the tissues of the body, is very potent and causes the other symptoms of the disease to appear. Another condition with which most people are familiar is lock-jaw, so-called from the effect on the muscles of the jaw of the poison produced by the tetanus bacillus, which is often present in remarkably small numbers for a disease of such potency.

The diphtheria bacillus was one of the first disease germs to be identified definitely, in spite of the fact that, since it is its toxin that causes the disease, the third of Koch's postulates was not so easy to demonstrate. One of Koch's pupils, named Loeffler, was the first to show definitely that this bacillus was always to be found in the throats of children who had died from diphtheria. He grew the *B. Diphtheriae* on a special medium, which is still much used and goes by his name, on which this particular germ grows better than most others. The bacillus is a slender, slightly curved organism which in a typical

culture occurs in little groups that somewhat resemble Chinese characters. On Loeffler's medium, which contains a mixture of blood-serum and broth, solidified by heat, the bacillus grows rapidly. The interesting thing about it, and one which makes it relatively easy to identify, is that when it is stained in certain ways it shows small granules which stain much more intensely than the body of the bacillus. In a culture on the blood-serum medium the appearance is quite characteristic of true diphtheria bacilli, so that it can be picked out from the other "diphtheroid" bacilli which occur in the nose and throat very frequently and which are not dangerous to man. In recent years improvements have been made on the media for growing *B. Diphtheria*, and many variations of the medium containing the metal tellurite are now used. On this, colonies of the diphtheria bacilli are black, or grey and black, and the bacteriologist picks them readily out of a mixture of germs.

As we have stated, Loeffler quite easily demonstrated that this germ was present in all cases of diphtheria; he expected to find it in all the organs of the body, since so many of them are affected in the disease, but he could discover them only in the throat. His first attempt to reproduce the disease in animals was not entirely successful, and it was some years later—in 1888—that two French workers, Roux and Yersin, demonstrated that the disease could be reproduced and that its effect on organs distant from the throat was due to a poison given off by the bacilli. The intense discomfort and occasional fatalities accompanying the local inflammation in the throat are only part of the disease; its most serious effects arise from the action of the poison on the heart and

on the nervous system. We now know that if *B. Diphtheriae* are grown in a fluid broth for some days, the broth becomes gradually saturated with the poison. If we use a fine porcelain filter we can remove all the living bacilli and obtain a filtrate which is sterile, but which contains the poison. Such a broth injected into man or animal will produce results similar to those of the disease. This fact is not only of importance as a proof that these germs cause the disease through their toxin, but also because it has enabled us to discover, to use, and to enhance the natural defences of the human body against germs. This development we shall deal with in a later chapter, for enough has now been said to show that many of the most deadly of the diseases that attack man are caused by disease germs, either directly or indirectly.

CHAPTER V

THE PRINCIPAL ORGANISMS AND THEIR EFFECTS

SINCE bacteria are of different sizes, shapes, and habits, and have different effects, one of the first problems presented to bacteriologists is to classify them. This presents difficulties comparable with those that meet the biologist, who endeavours to arrange all the known animals in their respective species. As the subject of bacteriology has developed, various classifications have been attempted, but none of them is simple enough to be given here. For our present purposes it will be enough to consider bacteria according to their shape and to note which of them are most important.

We shall consider first those germs that are spherical or nearly spherical, as distinct from those that are cylindrical or in one of the many forms in which the length is much greater than the width. The spherical organisms are known as "cocci," but quite a number of them are not strictly spherical and show a slight departure from this shape. Modern classification gives them names different from the true cocci, but we shall adhere to the common forms of their names without going into such fine details. The cocci are distinguishable from each other by their behaviour with Gram staining, by the arrangement of the cocci in relation to each other, by the size and style of colony they produce on ordinary media, and by their

behaviour when cultured under a variety of conditions. To-day our knowledge of the diseases which the cocci cause is fairly extensive, so that the source from which a particular germ is isolated is in itself an indication of the organism we expect to find.

Of this group the first are the cocci that are Gram-positive (i.e., stain dark by this method), and these are the staphylococci, streptococci, and pneumococci. The staphylococci we have already discussed as the cause of boils, noting that they form little clusters, and give fairly large colonies on plain agar, and that these colonies vary in colour. Streptococci, on the other hand, produce much smaller colonies as a rule, and under the microscope are seen to arrange themselves in chains like a string of beads. The chain varies in length with the exact type of streptococci and with the type of medium on which they are grown. The *Streptococcus Brevis*, which is often not harmful to man, grows on ordinary agar and gives chains so short that they contain only four to six cocci. The more usually dangerous *Streptococcus Longus* grows best in the presence of blood; when grown in broth containing glucose it produces very long chains. Among the streptococci there are some which will not grow in the presence of oxygen; many strains, most of which are of importance in relation to disease, have the power of "haemolyzing," or breaking down, blood. They cause many serious diseases in man, such as endocarditis (inflammation of the heart-valves), scarlet fever, and puerperal, or child-birth, fever.

The pneumococcus grows only in the presence of blood and is usually found as a "diplococcus," i.e. as two cocci lying together. These cocci are a little

longer on one axis than on the other, so that they are usually described as lanceolate in appearance. Under certain conditions it can be shown that each pair of cocci is enclosed in a capsule, a coating of some undifferentiated substance which can be made visible by staining with special methods. The chief disease caused by the pneumococcus is pneumonia, particularly the more serious type of that form of inflammation of the lungs; but it can also attack other organs. It is usually virulent towards man and particularly virulent towards small animals such as white mice, which are sometimes used to establish its exact identification because of this fact.

There are four principal members of the Gram-negative cocci. *Micrococcus Catarrhalis* is the most easily grown and it yields an easily visible growth of white colonies on all the ordinary media. It is to be found in the throat of almost everyone and it is very doubtful if it ever causes harm to man. When stained by the Gram method its appearance is usually that of a small red sphere, and it is fortunate that it can be separated from its companions in this group, as all the others cause definite diseases.

The two principal organisms of this group—the meningococcus and the gonococcus—both occur as diplococci and differ very slightly in size and shape, so that they cannot be distinguished with certainty by the microscope alone. In both cases we have, however, a strong, and indeed an almost infallible, indication as to which is which if we know the source from which they have been derived. The meningococcus causes cerebro-spinal fever, and although it may invade the blood stream and occasionally affect other organs, it is usually in the brain and spinal cord that

it is to be found. It is discovered by removing a sample of the cerebro-spinal fluid, by inserting a needle into the spinal canal, low down in the back. The gonococcus causes gonorrhoea, one of the venereal diseases, and it is therefore to be found in the pus which comes from the typical discharge. The gonococcus and the meningococcus both show a slight departure from the sphere, being bean-shaped,

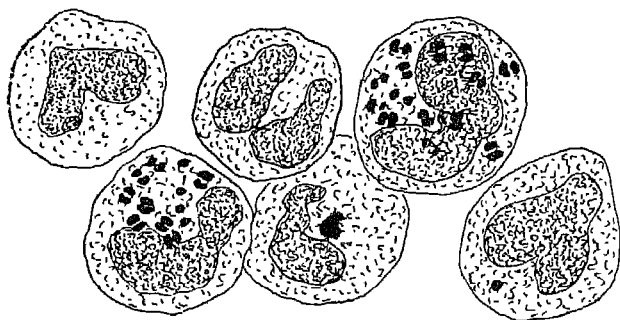


FIG. 4.—Pus cells destroy many germs and the gonococcus can usually be seen inside the pus cells.

the flatter surfaces facing each other in each diplococcus. One particularly interesting point about them is that they are found inside pus cells; of the two, the gonococcus is more usually found in this position and in large numbers. Pus, as we have already noted, is one of Nature's defences against bacteria, and the finding of the gonococci inside the pus cells is an example of phagocytosis (Fig. 4). The pus cells have taken up the organisms they seek to destroy. When the bacteriologist is looking either for the gonococcus or the meningococcus he uses a

medium containing blood, since both are somewhat delicate and difficult to cultivate.

There is a small group of organisms which were at one time classified as cocci, but which are now included in a special group since they vary considerably in size and shape, and, although often "coccoid," are not quite typical. These are the *Brucella* organisms, so-called from one of our famous British bacteriologists, and they cause two diseases of animals which are also dangerous to man. These are Malta fever, which infects the goats of that island and passes from them to human beings in the milk; and Abortion, or undulant fever, which in this country infects cows and occasionally passes by way of their milk to human beings. Fortunately this disease, while it causes serious illness, is seldom fatal. This group of organisms has one feature which is not particularly common: they grow better in the presence of more carbon dioxide than is usually present in the air.

The bacilli present a more complex problem than the cocci, for there are much larger numbers of them that are of serious importance, and they vary very considerably in size and shape and in their action. We have no space to consider in any detail those bacteria which do not form a simple cylinder, but occur as "spirilla" or spirochaetes; that is to say, organisms curving or having a wavy outline. The most important of these is the *Spirochaeta Pallida*, a very delicate organism only about 0.25μ in breadth although $4-14\mu$ long. It occurs in a corkscrew form with eight to twelve windings. This organism is the cause of syphilis and is exceedingly difficult to grow in artificial culture. It is found in the serous exudate from the primary lesion of syphilis and can be demon-

strated in the tissues in the secondary and later stages of the disease.

We may divide the bacilli, like the cocci, into those that retain the Gram stain and those that do not, but there is one very important group which lie outside this classification because they do not stain by Gram methods. These are the "acid-fast" bacilli, of which the most important member is the tubercle bacillus. We have already indicated that it can be stained by special methods and grows very slowly on its own special medium. The germ which causes leprosy is very similar in size, shape, and staining. Other members of the group are found in nature, but do not seem to affect man. One of them occurs in the vole, or water-rat, and is now used in an attempt to provide immunity in human beings against the whole group. Some success with this method has been claimed.

The bacilli that are Gram-positive form an exceedingly important group, and a large number of them are dangerous to man. Of these the *Bacillus Diphtheriae* has already been described, and its peculiarities of staining and its need for a medium containing blood-serum noted. There are a large number of diphtheroid bacilli, and sometimes it is difficult to be quite certain that a particular germ is a true diphtheria bacillus in the sense of being the real cause of disease. In such a case it is usual to test its virulence by injection into a guinea-pig, which is susceptible to the diphtheria toxin.

We have also mentioned *B. Tetani*, which, in addition to being Gram-positive and a toxin-producer, possesses the capacity for producing spores. When the bacillus produces a spore—which it does only

under certain conditions—there appears at one end a rounded body, so that the bacillus looks exactly like a drum-stick. Other and perfectly harmless bacilli have a similar appearance; consequently a virulence test may be the only means of distinguishing between them. As with the diphtheria bacillus, this involves the injection of the suspected tetanus bacilli into an animal. Another Gram-positive, and spore-bearing, bacillus which may also require a virulence test is *B. Anthracis*—the cause of anthrax in sheep and cattle and also in man. It was with *B. Anthracis* that Robert Koch made his first bacteriological experiments and proved both that the germ caused the disease and that it formed spores so highly resistant that they might remain on the grass in pasture for a very long time.

There is one group of Gram-positive bacilli which are of particular interest in relation to war injuries. These organisms invade the tissues through the injury and produce a condition known as gas-gangrene, because of the amount of gas they produce in using up the body fluids for their growth. The group is known to-day as the *Clostridia*, of which the most familiar is *Cl. Welchii*, which at one time was the constant source of anxiety to surgeons dealing with battlefield casualties, but which to-day yields almost entirely to modern methods of treatment by a combination of chemicals, sera, and efficient surgery.

The Gram-negative bacilli are the largest group of organisms, and nearly all of them cause disease in man. They have the most varied characters, differing in size over a wide range. They may be motile or non-motile, and, although most of them grow rapidly, a few can be cultivated only slowly and with special

media. Most of them produce white or translucent colonies, but some produce pigments. *B. Prodigiosus*, for example, yields a red pigment; it is the source of the blood colour on bread which gave rise to the supposed miracle of the "Bleeding Host." So wide are the variations in this group that many subdivisions are necessary, and the modern bacteriologist calls them by a variety of names. But in order to stress that they are all of cylindrical shape we are retaining the older title of bacillus for all of them.

One of the sub-divisions includes the group which are very small in size and grow only on media containing blood. For this reason they are often referred to as "haemophilus." The *Bacillus Influenzae* is the principal example of this type. It is found in many cases of feverish conditions called influenza, and it can be isolated from the throat and lungs of fatal cases, but it is no longer regarded as the cause of influenza. On suitable media it gives a growth of small transparent colonies; it is a very small bacillus, exhibiting to a marked extent another feature called "pleomorphism." This term means simply variation in shape. *B. Influenzae*, although almost always small, sometimes grows into larger and longer forms, especially if the culture is kept for some time.

The main group of Gram-negative bacilli are often spoken of as the colon bacilli, since so many are found in the colon—part of the intestine. Under the microscope these are all practically identical. They are fairly straight rods which vary considerably in size. Some are actively motile and possess flagellae which drive them through fluid media. On ordinary agar they usually give a heavy growth of colonies that are white or greyish. More elaborate methods

than have yet been described are necessary to separate them from each other.

The first of these methods is biochemical, being based on the fact that these colon bacilli all utilize or ferment sugar. When sugars (the chemist is concerned with many kinds of sugar in addition to the ones we familiarly refer to as sugar and use for most sweetening purposes) are fermented, there is usually a production of acid and often a production of gas. To demonstrate this effect, special media are prepared in which the sugars are incorporated. If we add to such media a dye, such as litmus or neutral red, which changes colour when the fluid changes its reaction from alkaline to acid or *vice versa*, we shall be able to detect at once if it has become acid. In the laboratory these sugar media are put up in tubes in which a much smaller test-tube has been placed mouth downwards in the medium (Fig. 2, p. 24). During the process of sterilization the heat drives all the air out of the smaller tube, which thus becomes filled with the fluid. If an organism growing in this medium produces gas the small tube will be filled with bubbles, and if it produces acid the colour will change.

The commonest colon bacillus, *B. Coli*, will produce both acid and gas in media containing glucose, lactose, and other fermentable substances; it does so very rapidly indeed. It is a most extraordinary and fortunate fact that the colon bacilli do not all absorb the same sugars, and in particular that they are sharply different in their behaviour towards lactose. The result is that the bacteriologists make a first division of these germs into those that ferment lactose and those which do not and are therefore known as the non-lactose fermenters. Thus, to give an example,

B. Typhosus, the cause of typhoid fever, does not ferment lactose, and while it utilizes glucose it does so with a production of acidity but no gas. Its very near relation *B. Paratyphosus* also does not ferment lactose, but it does produce gas as well as acid in the presence of glucose. In this respect it differs again from some of the bacilli causing dysentery, which may attack glucose but not the substance "mannite," which the paratyphosus does ferment. For the complete biochemical separation of all the organisms in this group a very large number of fermentable substances are required.

Even then the complete identification of all the germs in this group requires further tests. One of these tests—the serological—is mentioned in a later chapter. Among this group of organisms there are those usually described as the *Salmonella*, which cause food poisoning and are so nearly related to each other that in some instances an analysis of almost every detail of their structure is necessary in order to separate them. This development led, during the War of 1939–45 to the setting-up of special laboratories to which unusual organisms of this type could be referred in order that they could be named and their significance more clearly understood.

It should be realized that the *B. Coli* exists as a normal inhabitant of the human digestive tract in enormous numbers. Since the intestinal tract is also the seat of typhoid and dysentery, a simple method of separating the causes of these diseases from *B. Coli* is essential. In culturing a specimen of the patient's motion, advantage is taken of the behaviour of these organisms towards lactose. A solid medium containing lactose and a dye easily affected by small

amounts of acid are used. On a culture plate, such as in Fig. 2, separate colonies can be obtained, and those of *B. Coli* which have fermented the lactose will appear red, while the pathogenic *B. Typhosus* and all its relations appear white or colourless. In recent years solid media of this type have been highly developed by the discovery of substances which almost entirely prevent the growth of *B. Coli* without affecting the typhoid bacillus and the food-poisoning group; by using these substances rapid and accurate diagnosis can be made.

It is important to note that although *B. Coli* is normally present in the intestines and does not cause any harm, it can be quite a serious menace to health if it reaches other parts of the body. It may invade the urinary tract and cause severe inflammation of the bladder. In cases where, by disease or accident, the stomach or intestine has been ruptured, *B. Coli* escape into the abdominal cavity and cause peritonitis, which even to-day is a dangerous condition.

This description does not exhaust all the Gram-negative bacilli, but others will come into the story at a later stage. Before dealing with them we wish to relate another fact which is best illustrated by this group of bacteria. We recognize that they cause much harm to man, but they have enabled us to discover the wonderful power that the human body has to resist their activities, and from this discovery we have been able to devise methods both of preventing and curing the diseases they cause.

CHAPTER VI

MAN'S OWN DEFENCES

SURROUNDED as he is by germs, and coming into contact with them in everything he touches, in the air he breathes and in many kinds of food, man has clearly a need for many defences against micro-organisms. A full list of the microbic diseases and a description of their variety comes as a great surprise to many people, but it is at least equally surprising that in spite of this number and variety many people escape most of the diseases caused by germs and that many microbes we discover in connection with human bodies cause no harm. The reason for both these phenomena is that during his evolution man has developed a strong natural resistance to the invaders; and of course in modern times he has, by his scientific discoveries, added many methods of preventing or curtailing the attack of some of the most virulent germs.

Before an organism can cause its appropriate disease it must gain entry to the body. The two chief routes of entry are, as we have seen, the digestive system and the respiratory tract. Germs present in the air, in dust, or in those globules of moisture spread by every cough and sneeze, are sucked into the nose and lungs by every breath. Food and water carry organisms to the digestive tract, but many of these are normally destroyed by the digestive juices. It is exceedingly fortunate that these organs do not fall a

victim to every germ; they deal effectively with most of them, and it is only when some circumstance such as cold or exposure has lowered the natural resistance that they are able to start up an infection. When germs do pass the barriers in the lungs and the stomach, they come into contact with two weapons provided for the body by the blood stream—weapons which man now uses in his scientific battle against disease.

In animals and man the blood flows through the arteries to every part of the body, carrying foodstuffs and oxygen to the tissues, and it returns from them through the veins, carrying the waste products of the bodily metabolism. Blood consists not only of fluid, but of cells, the red and white corpuscles. The white corpuscles are of different kinds, but the majority have a nucleus made up of a number of lobes, and from this fact these cells are called "polymorphonuclear." These play an important part when the body is attacked by bacteria, for they have the power of forcing their way out of the blood stream into the tissues and of destroying the invading germs. In so doing they behave like the simplest form of animal life, the unicellular amoeba. It will be remembered that the amoeba consists of a single microscopic globule of protoplasm which moves by pushing out this protoplasm in finger-like projections or "pseudopodia." When one of these comes in contact with any substance suitable as food, the amoeba simply flows around it, taking the particles directly into its body and digesting them. So far as bacteria are concerned, the polymorphonuclear cells in the blood behave like amoebae and can engulf and digest bacteria within the body. If, as we saw in the case of a boil, bacteria have

entered the body, the polymorphonuclear cells become mobilized and pass out into the tissues and begin destroying the staphylococci. In this way pus is formed, and in many cases the phagocytes are strong enough to destroy all the disease germs, thus enabling the tissues to return to normal. Often, however, large numbers of pus cells are themselves destroyed in the process.

At one time it was thought that this was a sufficient explanation of how man got rid of disease germs of all kinds. But further study showed that while, for example, the pyogenic cocci are dealt with in this way, other germs are not "phagocytozed." When phagocytosis is going on in any part of the body, large numbers of polymorph white cells are needed to replace those destroyed in the struggle with the bacteria. This increase can be detected in any sample of blood, and the number may rise to five or ten times the normal figure so long as the disease is going on and the patient has still power to resist (Fig. 17, p. 135). In some diseases, however, of which one is tuberculosis, the number may not be increased; in others, of which typhoid fever is the most common example, the number may actually be decreased. In these disease conditions the poison produced by the invading bacteria calls forth no response on the part of the polymorphonuclear cells.

In recovery from such diseases another factor comes into play and the disease germs are actually destroyed or rendered harmless by the production within the body of "antibodies," substances which in one way or another render the germ inactive, ineffective, or actually destroy it. This effect is very clearly demonstrable in typhoid fever and other fevers caused

by Gram-negative bacilli. The typhoid bacillus infects the digestive tract and causes ulceration of the intestines. The general effect on the patient is profound, and the illness goes on for some weeks. During this time the body fights the disease by preparing an antibody to the typhoid bacilli, and this can be detected in the blood by what is known as the Widal

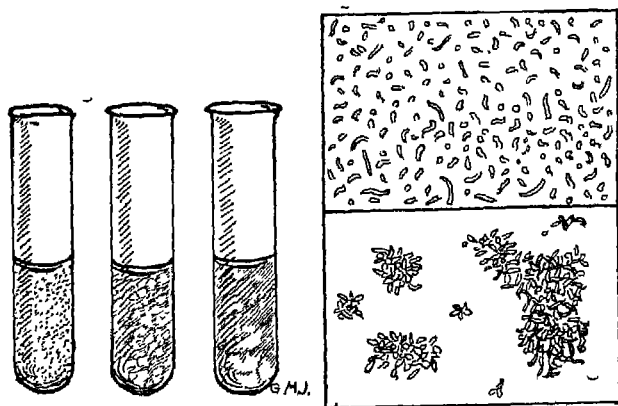


FIG. 5.—The Widal Reaction shows clumping of bacteria either in test tubes or magnified under the microscope.

reaction. In the early stages of the disease the amount of circulating antibody is very small, but after the tenth day it increases rapidly in amount and at that time the Widal reaction forms one of the most reliable tests in diagnosing the different fevers of the enteric group. The procedure is as follows:—some of the serum or clear fluid from the patient's blood is taken and diluted in various strengths; each is then mixed with some known typhoid bacilli suspended in fluid.

This mixture of serum and organisms is kept at a temperature of 56° C. for one hour. At the beginning of the hour the bacilli are so evenly dispersed in the fluid as to give a uniformly turbid appearance with no deposit. If the Widal reaction is positive at the end of the hour, the bacteria will be found at the bottom of the tube "agglutinated"—that is to say, formed into small clumps which can be seen very easily when the tube is shaken (Fig. 5).

The process of agglutination can also be seen under the microscope, and, although the complete Widal reaction necessitates the setting out of a number of dilutions, a simple spot test can be made on a slide with the serum itself. Under the microscope the bacilli, which are at first uniformly suspended, can be watched coming together and forming clumps.

It has further been found that if some dead typhoid bacilli are injected into an animal or man, the blood will show, by the same technique as the Widal reaction, that antibodies have been formed. If sufficient injections are given to stimulate the production of a large amount of antibody, there will be created an immunity, i.e. complete resistance to the disease. This discovery was first tested out in the Boer War and used during the two major world wars; during them its value has been convincingly demonstrated. To practically all soldiers a series of injections of typhoid and other organisms is now given, and the routine use of such a "vaccine," as it is called, has enormously decreased the danger to fighting men from the diseases concerned. The word "vaccine" is derived from the fact that smallpox (*Vaccinia*) was the first disease in which immunity was artificially produced. In smallpox, however, it is not an emulsion of dead germs

that is used; the patient is given a mild attack of the analogous disease, cowpox.

Another variation of the process is found to be effective in rabies, or hydrophobia. This disease, which was very prevalent in this and other countries before dogs were brought under quarantine and control, attacks the nervous system. Even if a person has been infected by the bite of a dog, the disease can be prevented by injections of brain matter from animals previously infected by it and therefore assumed to contain a certain amount of the agent which causes the disease.

These are all examples of "active" immunity. The material injected or otherwise introduced into the tissues causes the body to produce its own antibodies, which we can then observe circulating in the blood stream. It follows, therefore, that if such blood is taken and injected into another patient suffering from the disease, the antibodies will assist the sick person in his fight against the disease. If we inject enough antibody to cure the disease, the patient has been given a "passive" immunity, which may be sufficient to tide him over the attack but may not produce such a permanent immunity as does active immunity. The blood which is used to introduce these antibodies may of course come either from a man who has had the disease or had injections or from an animal which has been artificially immunized.

The importance of this method of treatment is perhaps best illustrated in those diseases which are caused not so much by the invasion of the tissues by the germ itself as by the poison which it produces, for example, in diphtheria. The toxin produced by such an organism circulates in the blood stream, as

we have already described. When we grow these bacteria in a fluid medium they produce their toxin just as they do in the body, and this can be isolated in a fairly pure form. If the toxin is injected into an animal, it reproduces the symptoms of the disease. When injected in quantities too small to cause serious injury, the animal tissues are stimulated to produce antibodies, and after a number of such injections the amount of antitoxin produced rises to a high figure.

From the blood of such an animal a serum can be prepared and used to protect human beings. In the case of diphtheria, antitoxin is the recognized and most effective form of treatment. The antitoxin used in this disease is usually produced from horses. Another animal serum so produced affords protection against tetanus. The germs of this disease are introduced into the body in dirt, particularly after accidental injuries, and its toxin is particularly dangerous to the nervous system. Fortunately the antitoxin which can be produced is very potent and neutralizes large amounts of the poison. If given speedily enough it can prevent symptoms of the disease from developing. This has, during two world wars, resulted in a great diminution in the number of cases of tetanus, which was formerly very prevalent after battle injuries.

Mention has been made of giving injections of dead bacilli in order to produce an artificial immunity. In cases where the germ produces a toxin, small amounts of the poison itself can be injected, resulting in the production of antibodies. Methods have been found by which the toxin can be so modified that it is no longer dangerous to human beings and yet has the power of producing antibodies very rapidly. Thus

in diphtheria a toxoid (which usually means the toxin combined with alum) has been prepared of such potency that two small and harmless injections produce sufficient circulating antibodies to render the patient immune to diphtheria for some time, and fairly safe from its worst effects for many years if not for the whole of life. In tetanus a toxoid is also used, and most men who were injured in the war owed their freedom from this disease to the injection of the tetanus toxoid they had earlier received.

The human tissues will produce antibodies to a great variety of substances; materials which cause antibody production are known as antigens. As a rule the body produces only the antibodies to the substance introduced into the body. Thus an injection of *B. Typhosus* will cause a production of antibodies to *B. Typhosus* but not to the closely related *B. Paratyphosus*. The exact diagnosis of these related diseases may indeed depend on this fact, and the Widal reaction as usually carried out in the laboratory consists of testing the patient's serum against not only *B. Typhosus* but *B. Paratyphosus A* and *B*.

Occasionally, however, the antibody is not specific against the infecting organism. For example, in typhus fever, which is caused by a disease agent known as a *rickettsia*, the blood reacts with emulsions of *B. Proteus* (Weil-Felix reaction), although that organism has really nothing to do with the disease. In syphilis the Wasserman test, on which we rely mainly for the confirmation of the diagnosis, depends on the reaction of the blood with a solution of the lipid bodies in heart muscle. These lipid bodies are present in all muscles and are extracted by treating the heart muscle with ether and alcohol. So far no

explanation has been found for this peculiar reaction with a substance from normal tissues instead of with the infecting agent. It is, however, so specific that a really positive result is absolute confirmation of the tentative diagnosis.

When either active or passive immunity has been produced, the body will for a time be able to avoid infection entirely. Unfortunately this immunity does not necessarily last for a long time. It may, as in smallpox, last for years, or it may last for a few days only. There are indeed some diseases in which an attack appears to have the opposite effect and to render the victim more susceptible to the disease. This may be due to some peculiarity in the chemical composition of the particular germs concerned.

On the other hand, certain chemical substances have been isolated from the body of some germs which are capable of acting as antigens, and it is probable that in the end methods will be found by which active artificial immunity can thus be given against most germs if other weapons, which we shall discuss in the next chapter, should fail.

CHAPTER VII

NEW WEAPONS AGAINST BACTERIAL DISEASE

THE problem which medicine has faced through the ages has been to discover antidotes to the diseases caused by germs. This struggle began long before the actual existence of bacteria had been demonstrated. Indeed, doctors had even then achieved a number of successes against some parasitic enemies, fairly complete as in the case of malaria, and partial as in the case of syphilis. No sooner had the science of bacteriology been established than the hunt for an efficient method of dealing with germs became the aim of all medical research workers. It is of particular interest that the first attempts aimed at harnessing the natural defences of the body; Pasteur was particularly alive to this possibility. During the first twenty years of bacteriology an immense amount of work on natural and artificial immunity was carried out, and great advances were made in the treatment of some diseases by serological methods. In these the blood of animals that had been immunized against particular germs was used, as it is still used to-day in the treatment of human disease.

It will be recalled that Lister used carbolic acid in various forms to make surgery safe by destroying the germs that usually entered surgical wounds in hospitals and made operations so dangerous at that time.

Carbolic acid, while effective, was not a safe or perfect antiseptic, and from his day to this the chemist has been searching for the ideal substance with which to destroy the germs dangerous to man. The ideal substance would, of course, be one which destroyed all germs, which could be injected into the human body or taken by mouth and absorbed in the digestive tracts, and which had no poisonous or toxic effects on the tissues of the human body. The ideal substance has not yet been discovered, but advances towards it have been made at an ever-increasing rate in recent years.

The number of substances now known to have an antiseptic action is very large indeed. Many chemical substances are available for use outside the human body in the destruction of germs. These antiseptics are of very varied chemical composition, and their strengths vary in different circumstances. Many can be safely used on the human skin, and some are sufficiently harmless to the tissues to be used in the form of dressings for wounds, but most of these suffer from the disadvantage that the tissue fluid, serum, and pus lower their antiseptic effect. Those that destroy germs by killing them through chemical action are least efficient when they are in contact with the tissues or tissue products, with which they also unite chemically, thus being rapidly rendered inert.

One of the greatest of the research workers who sought to solve this problem of discovering a chemical substance which could destroy bacteria and other parasites without harming the tissues of the human body was the German scientist Ehrlich. He discovered, after laboriously testing hundreds of sub-

stances, that arsenic could be combined in such a form with other chemicals as to produce a substance with very little harmful effect on normal tissues but capable of destroying the germ of syphilis. This discovery, momentous in itself, was much less than Ehrlich had hoped for when he began his search. Theoretically, he argued, it should be possible to discover a substance that could destroy all the bacterial enemies of man without harming man himself. Since his time, other arsenical preparations, better than the first one he discovered (which has long been known as 606) have been found, and as a result the *Spirochaeta Pallida* has lost some of its power.

It will be recollected that syphilis is one of the most dangerous of all bacterial diseases. The spirochaete which causes it not only produces damage to the tissues at the point where it enters the body, but it spreads rapidly through every organ and it continues to live in the body for many years. Some of its effects may not be produced until long after the original infection, and in addition this germ can pass from the mother to the unborn child, in which case it causes death or disease.

The discovery by Ehrlich did not solve the problem of the perfect antiseptic, but it did demonstrate that powerful antiseptics could be made in the laboratory and it stimulated an immense amount of new research in this field. The chemist to-day can take a substance which has been proven to have some effect and, by making small changes in its composition, prepare entirely new substances which may have the beneficial effect of the first product without any of its harmful ones. The number of substances so manufactured and tested is now uncountable. The proportion of

successes has been small, but in recent years there have been, among these successes, one or two that have changed the whole relationship between the scientist and his bacterial enemies.

One of the first triumphs was the discovery of a series of drugs—of which acriflavine, a yellow-coloured substance soluble in water, is probably the best known—which have an exceedingly powerful effect against the majority of the common germs. This particular antiseptic is most valuable on the surface of the body, and since it is very lethal to germs, even in small amounts, it was a great disappointment that it did not turn out to be the perfect antiseptic for internal uses.

It will be recollected that one of the most dangerous germs is the streptococcus, particularly when it gives rise to puerperal fever following child-birth. At one time many women died from "child-bed fever," and it was a long time before doctors realized that this disease was due to a virulent form of the streptococcus. It is a germ that may be caught and carried by almost anyone, and while it may be present in or on the body without causing disease, because of an existing immunity, it may find ideal conditions for its growth and spread in the woman who has lost blood and has been weakened by the birth of a child. Bacteriologists who were testing substances against this particular germ suddenly discovered one which had the power of killing it even when present in exceedingly small amounts. No sooner had the fundamental discovery been made than chemists and bacteriologists all over the world produced a whole range of new substances of similar kind, which not only proved effective against the streptococcus, but also against many other dangerous microbes.

These drugs are usually referred to as the "sulphonamides" or, in colloquial language, the sulpha drugs. The first one which proved to be really effective was sulphanilamide, which is of particular use against the type of streptococcus which causes puerperal fever. It is, however, not without some toxic effect in human beings, and it is not particularly effective against other germs. Consequently the chemist continued his game of making changes in the molecular structure of the drug in order to develop new substances. The hope of the perfect antiseptic was carried a stage further by the discovery of a similar drug—soon to be known all over the world as M. and B. 693, though more correctly described as sulpha-pyridine—which was not only effective against the streptococcus but very efficient in dealing with the pneumococcus. This Gram-positive diplococcus we have already noted as the chief cause of pneumonia, which has always been a difficult condition to treat and one with a high mortality. Within a very short time of the demonstration in culture and by experiment in mice that sulpha-pyridine could destroy the pneumococcus, the lives of human beings were being saved by its administration. Once again, however, we had the same story. It was not effective against all germs, and it sometimes upset the patient and produced dangerous reactions. So the chemist continued his search.

To-day there are in common use six or seven other sulpha drugs, all effective against many of the Gram-positive cocci, against some of the Gram-negative ones, such as the gonococcus and the meningococcus, and also effective against Gram-negative bacilli, such as *B. Coli* when it causes cystitis or infection of the urinary bladder. By the use of these drugs many

conditions that were formerly dangerous to health and to life have come almost completely under control. These drugs have the great advantage that they can be taken by the mouth and absorbed into the blood stream from the alimentary tract and reach every part of the body. But all of them are still occasionally dangerous and still have their failures.

The next great discovery was to come in quite a different field as a result of a chance observation combined with one of the greatest examples of applied scientific research yet carried out in the medical field. This was the discovery of Penicillin, the greatest romance of modern medicine and one that is not yet ended.

From the earliest days of bacteriology it had been noted by bacteriologists, including Pasteur, that occasionally a germ turns up in culture which appears to have an inhibitory or antiseptic effect towards other germs. Inhibition, the prevention of growth, is more common than a direct lethal effect. Over a period of years many such observations were made and examined, and efforts were continuously conducted to discover whether this effect could be used for the treatment of disease. All of these earlier observations came to nothing, and the one we are about to describe might have suffered the same fate but for the advent of the second World War. It was about 1928 that the original observations on *Penicillium*, a type of fungus which is very common as a contaminant in bacterial cultures and as a mould in foodstuffs, were made by Sir Alexander Fleming. He reported that on one of his plate cultures of the staphylococcus a colony of *Penicillium Notatum* had appeared by chance and had had the effect of preventing the growth of staphylococci near it. As with

all other such chance observations, he carried out many experiments and confirmed that this fungus, in the course of its own growth, produced a substance which, in cultures at least, had the effect of preventing the growth or of destroying certain other germs. The substance proved difficult to isolate and to separate from the fungus, and because of this the early attempts to use it as a possible means of treating infections in patients failed. Under laboratory conditions it was easy to demonstrate its effect, but under conditions in which the human body was affected by bacteria it seemed impossible to achieve the same result against the invading germs.

When we were threatened with another great war, and large numbers of casualties were to be expected, an intensive search for the most perfect antiseptic began. It led another research worker, Sir Howard Florey, to make a further effort to isolate from the *Penicillium* this substance which, for some unknown reason (for there is, as far as we know, no connection between the fungus and other germs), can prevent the growth of various bacteria. It was no easy job to isolate this substance, to retain its potency, to purify it, and to obtain it in a form in which it could be tested out in animals and in man, but the British workers who were entrusted with this task carried it out successfully. From the fungus, grown in liquid media, was isolated the substance which we now call Penicillin, which has proved to be the nearest approach to the perfect antiseptic that has yet been discovered. In the most minute quantities and under all sorts of conditions, in the body cavities and in the circulating blood, it is lethal to a wide range of man's invading enemies. It is still a substance difficult to isolate and

purify; it is still something of a mystery in its composition; but it has already saved thousands of human lives and cut short hundreds of thousands of cases of dangerous disease (Fig. 6).

Penicillin has the widest range of any antiseptic that can be used within the human body, and it is particularly powerful against many of the Gram-positive organisms. Since we already had the sulpha drugs to use against streptococci and pneumococci, the greatest benefit of Penicillin is that it is particularly

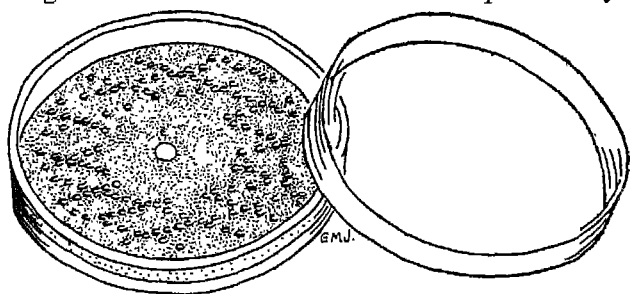


FIG. 6.—When germs are spread evenly over a plate of culture medium and a drop of penicillin placed in the centre there is a large area around it in which no germs grow.

effective against the staphylococcus. Even the most recent and the best of the sulphonamides had little effect against the staphylococcus, and in this field Penicillin is therefore a great advance. It is also remarkably potent against the group of Gram-negative cocci and produces the most sensational cures in gonorrhoea. It is possible that Penicillin acts, not as a direct poison to the protoplasm of the germs it destroys, but by interfering with their metabolism and growth. At first it was thought that this interference might be related to the substances which make some

germs Gram-positive, but its action against the Gram-negative cocci shows that another explanation has still to be sought. It is not effective against the Gram-negative bacilli such as *B. Coli*.

The discovery of this remarkable antibiotic, as Penicillin and other similar substances are known, has set bacteriologists in every country searching for other germs that exercise a similar effect. Already many organisms have been discovered which have the power of producing substances which have some effect against other germs. When the difficult process of isolating and purifying these antibiotic substances has been completed, some of them may form rivals to or improvements on Penicillin.

The greatest search is for a material effective against the tubercle bacillus, which has so far resisted all efforts. Indeed there is a triple race going on in the laboratories of the world to find an effective remedy for tuberculosis, and above all to find an effective preventive method. In the latter field injection of B.C.G. Vaccine, as carried out in Sweden, appears to offer high hope—at least in persons such as nurses, doctors, and the children of the tuberculous, exposed to extra danger—of building up immunity and so preventing the disease.

In the field of cure the race is between those who elaborate and test new synthetic chemicals and those working with antibiotics. Of the latter, Streptomycin is known to have some beneficial effects but has not the almost fool-proof record of Penicillin. Among chemical substances some have been found that protect laboratory animals but are not yet applicable to man. Nevertheless, as this brief outline indicates, man is always making progress against even his most dangerous bacterial enemies.

CHAPTER VIII

ALLIES OF GERMS AND PARASITES

THE discovery of Penicillin reveals a curious natural phenomenon—namely, that one particular type of fungus should be able to produce a substance which is inimical to a whole range of bacteria. There is no reason to suppose that this ability on the part of *Penicillium* has an actual purpose in nature, for there is certainly not the kind of relationship between the fungus and germs dangerous to man that would lead to such a development. On the other hand, there are a great many cases in which germs capable of causing disease, or even death, could not force their way into the human tissues were they not assisted by other agents. To call these assistants “allies” is perhaps wrong, since there is no active joining of forces. Indeed, in some cases the agent which assists the bacteria to attack human beings is itself attacked by the germs. We know that bacteria cause disease in many of the lower animals, in birds, in fish, in insects, and even in plants. It is therefore obvious that, in coming into contact with all these natural objects, man must at times come in contact with the bacteria causing disease in these other forms of life. Indeed we come in contact in this way with many germs that are not harmful to man; but in many cases man is even more susceptible than the lower forms of life.

In quite a number of instances man is in this matter his own chief enemy, because a great risk of infection

arises from insanitary habits. In the more civilized countries this risk, together with many of its attendant diseases, has almost disappeared, but in a country like India epidemic diseases have every chance to spread. Water, whether for drinking or washing, is one of the most efficient vehicles of disease. Contamination with sewage or human excretion may pollute a whole water supply with the bacilli of cholera, typhoid, or any of the related germs. The cholera bacillus, it should be mentioned, is a Gram-negative bacillus usually spoken of as a "vibrio," the term applied to curved or comma-shaped organisms. It is an organism which grows very easily and is actively motile in water. It is present in enormous numbers in the excreta of patients suffering from the disease, and it may live for some time in water.

Food is another vehicle which may carry to man disease germs or their poison. There is a whole group of organisms, all Gram-negative bacilli, closely related to the paratyphoid family and generally spoken of as "the food-poisoning germs." Localized outbreaks of food-poisoning are usually caused by one or other of this group, and salmonella infections (as they are more accurately described) are fairly common even in an urbanized population. The identification of these organisms often depends on a reaction similar to the Widal reaction, which, as has been stated, consists of mixing the blood serum of a patient with a known strain of the suspected bacilli; should the blood contain antibodies the bacilli will be agglutinated. The same phenomenon is utilized in the reverse direction. A bacillus thought to be, for example, *B. Paratyphosus B* is mixed with serum from an animal previously injected with a known *B. Para-*

typhosus B and therefore containing antibodies to that germ; if agglutination occurs, then the identification of the bacillus is complete. One of the chief tasks of the modern bacteriologists is the rapid identification of such germs and the detection of the particular item of food which had acted as the carrier, so that the outbreak can be reduced to the smallest possible proportions. During the war special laboratories were set up for this purpose and they still serve as consultative laboratories for the bacteriologists.

Some of these germs are, however, carried a long time by a patient who has suffered from the disease they cause. In the last few years a very common complaint has been due to the Sonne bacillus, which usually causes a short, sharp intestinal attack from which the patient immediately recovers. This does not mean, however, that all the bacilli have left the body, for such a patient may retain them for many weeks. The danger in this is obvious. It means that any person carrying such a germ and handling food may unconsciously convey the germ to others. Legislation will probably be introduced to make the bacteriological examination of food-handlers compulsory.

In addition to this Gram-negative group of bacilli there is one of the Gram-positive type which infects food occasionally and causes severe illness and often death in man. This is the *B. Botulinus*, which produces a very powerful toxin and need be present only in very small amounts to affect the whole nervous system. It is an organism which produces spores; these are very resistant to heat and may therefore survive the process of cooking. They have been found in preserved meats.

The tubercle bacillus may be conveyed in meat from an animal which has suffered from the disease, but the chief carrier is, of course, milk. Modern regulations and hygienic methods of handling have diminished the number of samples of milk containing tubercle bacilli, but in milk which is not pasteurized the proportion is still too high. Another method by which the tubercle bacillus reaches the human body is through the expectorations of those suffering from lung tuberculosis. The bacilli may be present in quite large numbers in moisture coughed out of the mouth, and they may continue to exist for quite a long time in dust. It is of interest to note that there is a difference between many of the strains of tubercle bacilli found in milk and those present in human sputum. By various tests it can be shown that there are at least two types—bovine and human—which infect man.

Other animals also play their part in conveying disease. In the island of Malta, where goat's milk is extensively used, a feverish illness, known as Malta fever, frequently occurs. This is due to a small Gram-negative organism. In this country there occurs another disease, very similar to Malta fever and due to a very similar but not identical germ, the *Brucella Abortus*. This undulant fever, as it is called from the way in which the fever rises and falls, is usually contracted from the milk of cows which have also suffered from an infection by the same germ.

Undulant fever is not particularly dangerous, although it goes on for a long time, but there is another disease of sheep and cattle—namely, anthrax—which can be very dangerous. This is a septicaemic disease—i.e., one which infects the blood stream and

causes what is popularly known as blood-poisoning; the germ passes into the blood stream and is carried throughout the body and is to be found in most of the organs. The *B. Anthracis* is a Gram-positive organism which is somewhat rectangular in shape and, under certain conditions, contains a central spore. It has been found that the spores never form when the organism is growing in the body tissues. They appear in organisms outside the body under aerobic conditions, when there is plenty of oxygen present. These spores are very highly resistant and live for a long time in dust or on the skin and hairs of animals. As the spores resume the bacillary form when once inside an animal body, the disease spreads easily among animals grazing in an infected field. Man is also infected, as a rule through the handling of animal skins and in particular by the use of unsterilized bristle shaving-brushes. The spores may also be present on wool; workers handling this may, by inhaling small particles, acquire "wool-sorter's disease."

So far we have mentioned only diseases in which the ally of the germ has been entirely passive. There are many others in which the ally is passive in the sense that the conveying of the disease germ fulfils no purpose in the ally's own life; it is a mere accident that, in pursuing their active lives, they actually introduce bacteria directly into the bodies of human beings. Insects, fleas, ticks, lice, and mosquitoes all belong to this group, and the diseases they carry are among the most formidable man has to face (Fig. 7). It is an interesting point in natural history that so many parasites have developed a life-cycle which depends upon the inter-relation between two or more hosts.

Perhaps the most commonly known of these insect-borne diseases is malaria, in which the fact that insects feed upon the blood of man has enabled the *Plasmodium* (as the organism is called) to develop one of the most elaborate of all life-cycles, for the completion of which it must pass from the body of man to that of a mosquito and back again. All the

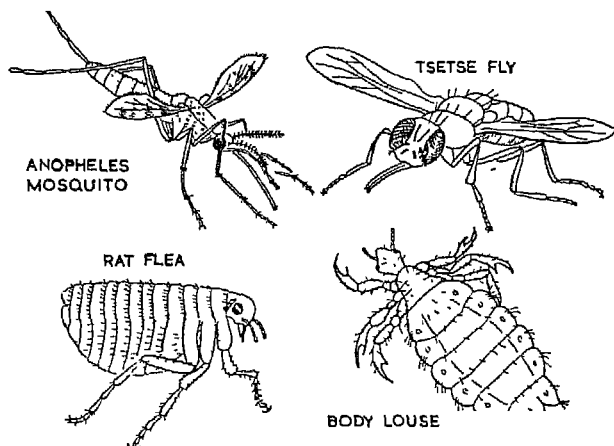


FIG. 7.—Insects that carry parasites

mosquitoes that we know do not carry the parasite, although there is more than one type that may do so. The life-cycle is not a simple straightforward development with two stages, one in each host for, in addition the malaria parasite can exist in one of its forms for a long time and in that form multiplies over and over again inside the human body. That particular stage is asexual, and it is because it has a very definite periodicity that malaria in the human being takes the

form of recurrent attacks in which temperature is an outstanding feature. There are several kinds of malaria, and the periodicity is different in each kind. During this asexual phase the parasite lives inside the red blood cells, which in its process of growth it destroys, leading to anaemia. Inside the red cell the parasite grows larger and larger, then divides up into

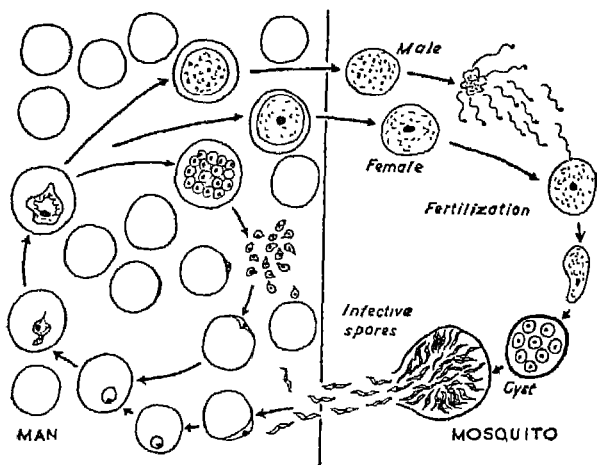


FIG. 8.—The life-cycle of the malaria parasite requires two hosts, man and the mosquito.

many smaller forms, which are suddenly liberated into the blood stream and immediately take up their abode in other red cells. The first stage in the development of the malaria parasite is as a small ring which can be recognized under the microscope (Fig. 8).

There are, however, among these parasites two different kinds, male and female, and they can unite to reproduce by a form of sexual union. This does

not take place in the human blood, but only when the parasites are transferred to the body of the mosquito. In biting through the human skin the mosquito takes up some of the blood; the male and female parasites come together and, following their union, hundreds of embryos develop in the body of the female insect. This takes place in the stomach of the mosquito; but the young embryos that develop find their way into the salivary glands of the insect, and from there are discharged into the human blood when the mosquito bites. From that point the remainder of the cycle in the human body continues on either the sexual or the asexual plan according to whether the parasites again pass to a mosquito or not.

Malaria is, of course, a very serious disease, and some of the great catastrophes that have overtaken civilization in the past may have been due to attacks of some such disease wiping out a whole population. That this is not improbable was shown by the epidemic which occurred in Ceylon as recently as 1934. The disease spread with amazing speed, and it is believed that over 100,000 deaths occurred. Apart from such fatalities, malaria is a particularly debilitating disease which can sap the energy of a whole community.

Since we know the life-cycle of the malaria parasite we should be able to interfere with it effectively. For centuries it has been recognized that the drug quinine has a markedly curative effect, once the disease has been established, and is also very effective in prevention. In recent years new synthetic drugs have also been discovered which destroy the parasite; and such substances as Mepacrine and Paludrine are now regularly used in the treatment and prevention of this

disease. Those who visit malarial countries are usually instructed to take every day a certain number of tablets of one or other of the drugs.

However, there are other methods of dealing with the disease. When the mosquitoes are destroyed in sufficiently large numbers in any particular area, the case-rate of malaria is quickly reduced. Among the methods used for destroying the mosquitoes are general improvements in the sanitary conditions of those areas where malaria is very common and efforts to improve the general health of the community by better nutrition, housing, and so on. More specific methods are also utilized and include spraying any stagnant water with oil, because the larva of the mosquito which exists in ponds and marshes cannot breathe through a film of oil. Other methods are the cutting away of vegetation from streams and pools and establishing better drainage, so that ultimately there are no places in which the mosquitoes can breed.

There are quite a large number of other diseases conveyed by the bite of insects; most of them are to be found in tropical and sub-tropical countries. They are discussed more fully in the next chapter, but we should note here a bacillary disease which at one time was exceedingly widespread and is conveyed by the flea. This is "plague," one of the worst of all infections. It is caused by the *B. Pestis*, a small round-ended bacillus which stains Gram-negatively. When it is stained with a simple dye like methylene-blue it gives a very characteristic picture. In ordinary cultures it shows marked plemorphism—that is to say, great variation in shape—some bacilli being long and slender, while others become very fat and irregular. It does not form spores, and has not

therefore the resistance of some of the other germs we have mentioned.

This organism infects small rodents and is found particularly in rats. The fleas, which appear to be always present on the rat, become infected with the bacillus and may leave the rat (especially when it dies from the disease) and change to a human host. When the flea bites, it always regurgitates some of the bacilli which have multiplied in its stomach. These enter the skin and spread rapidly through the body. They cause two distinct types of the disease, the more common being "bubonic plague," which in earlier times devastated large populations. In this form the lymphatic gland near the infected bite becomes inflamed, accumulates large numbers of the bacilli, and gradually breaks down. The other form, known as "pneumonic plague," chiefly attacks the lungs. While the normal method by which plague is spread is by the agency of the flea, in the pneumonic type the germ may pass from one human being to another as the result of coughing and spitting.

Another insect, the louse, carries an important and deadly disease—typhus fever. Here again we have an organism which infects both the rat and man, and it is in the rat that the disease continues to exist during the intervals between the epidemics which still occasionally sweep through countries. The disease is as deadly to the rat as it is to man, and on the death of the rat the lice look for a new host and may find it in a human being. Typhus is therefore closely associated with bad sanitation and overcrowding, and it has always been very common during war-time. It has been known for at least 800 years, and Zinsser, in his entrancing book, *Rats, Lice and History*, claims

that it has had more effect on history than the intentional actions of mankind. Only rarely is it seen in this country, but so long as it exists anywhere in the world, and so long as the rat exists in large numbers in or near human habitation, it is a disease which may at any time rear its head. During the recent war great strides have been made in reducing the danger from typhus. On the one hand vaccines have been developed which build up the immunity of the individual, and on the other hand the discovery of D.D.T. (the insecticide which effectively destroys the body louse of man and other animals) has reduced the danger of infection.

Enough has been said to make it clear that pathogenic bacteria have many opportunities of reaching the human tissues and causing serious illness. There is no need to ask ourselves how organisms assumed this habit, for it is clear that within the human tissues, warm and plentifully supplied with foodstuffs, the germs and parasites find ideal conditions for their growth and development.

So far we have been speaking of microscopic sources of disease, but there are quite a number that are relatively large and some which belong to a higher stage in the development of living things than the very lowly forms we have discussed.

CHAPTER IX

PARASITES

IN seeking the warm and nourishing conditions of the human body, parasitic organisms try to gain entry in a variety of ways. Clearly one of the simplest is through the stomach and alimentary tract along with normal foodstuffs. This wide portal of entry has proved extremely useful to certain animals of the worm type, which inhabit human intestines and spend the greater part of their existence there. In that position they feed upon the human body and grow to full sexual maturity; their ova (eggs) then pass from the body in large numbers and in a variety of ways infect other animals or other men.

Such parasitic worms vary over a very wide range in size, shape, and habits (Fig. 9). The best known are perhaps the tapeworms, which are found in most of the domestic animals associated with man and also in certain fish. There are a number of different types of tapeworms with slightly different habits of life. In some cases the ova may pass direct from the animal to man, as in the case of those infecting the dog, or they may be present in meat taken as food, such as pork. At certain stages of its life-history the worm passes into the muscles of the host; in this form it is ingested by the human being. In man the worm normally passes the whole of its life in the intestine, but sometimes it gets into other tissues, such as the liver or the lung, where it may produce large cysts, containing many parasites at one stage of their de-

velopment. These cysts very often become inert and may be shut off and calcified, surrounded by a layer of hard material and therefore no longer capable of spreading infection.

The tapeworm, as its name implies, may be of great length and is of a tape-like appearance. It is attached

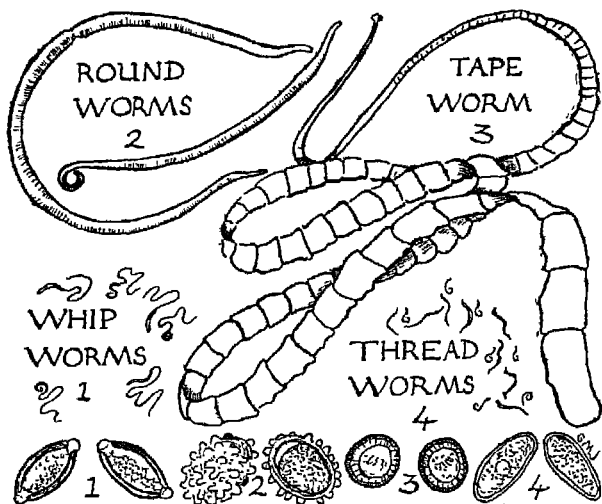


FIG. 9.—Parasitic worms and their eggs. The four commonest types are shown, but not to scale.

to the intestinal wall by an exceedingly small head either with a hook-like structure or a sucker. Behind this head there are segments which grow larger and more mature the farther they are from the head. To a certain extent each segment is a separate entity, developing slowly until at a later stage it becomes completely filled with mature eggs. The eggs are shed into the alimentary tract and so pass out of the body.

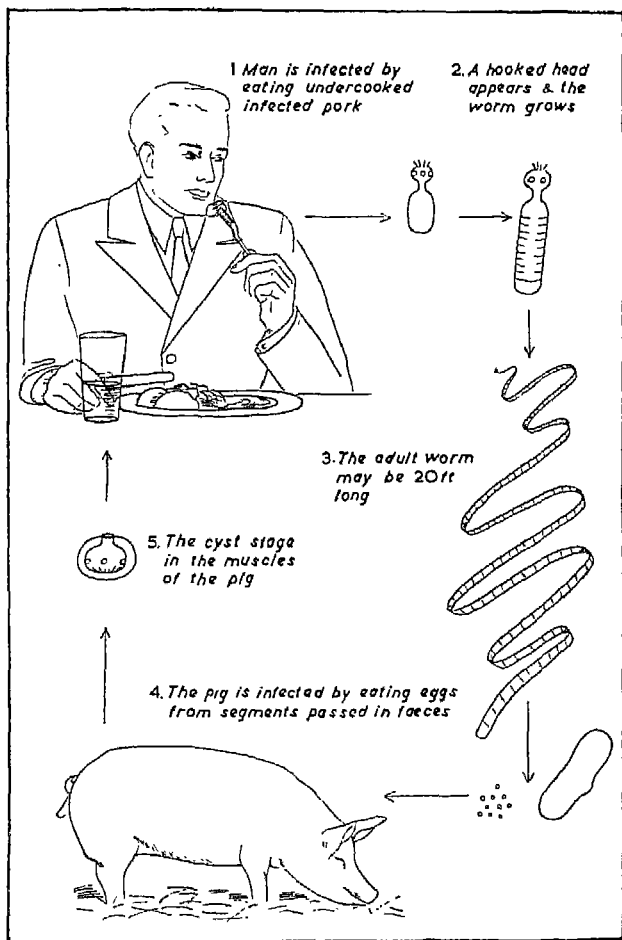


FIG. 10.—Life-cycle of Tapeworm.

The segments are hermaphrodite, both male and female, so that each is capable of reproducing the species.

The form in the intermediate host—the animal other than man in which part of the cycle is spent—is of course in no way like the tapeworm, which may be anything up to twenty feet in length when fully developed in the human intestine. The larvae do not remain in the intestines of the intermediate host, but pass into the muscles. The two types most common in this country reach the human being through either pork or beef which has been infected, and which has been incompletely cooked so that the larvae in the muscle have been able to survive (Fig. 10).

Another relatively common type of intestinal parasite in this country is the roundworm, which is very similar in size and shape to the ordinary earthworm, although it may sometimes be as long as twenty inches. In this case there are both male and female worms, the male being much the smaller of the two; the eggs are most commonly passed from the one person to another by means of contaminated drinking-water. It is usual for fairly large numbers of roundworms to be present at one time (Fig. 11).

Another common worm which is also of the earthworm shape is the threadworm, which, as its name implies, is of very small size and in appearance suggests small pieces of cotton. This also requires the presence of both male and female for the production of fertile eggs, which may be transmitted from one person to another in water or with uncooked vegetables. The whipworm, which we have also shown in Figure 9, because of the interesting type of egg which it produces, is another fairly common

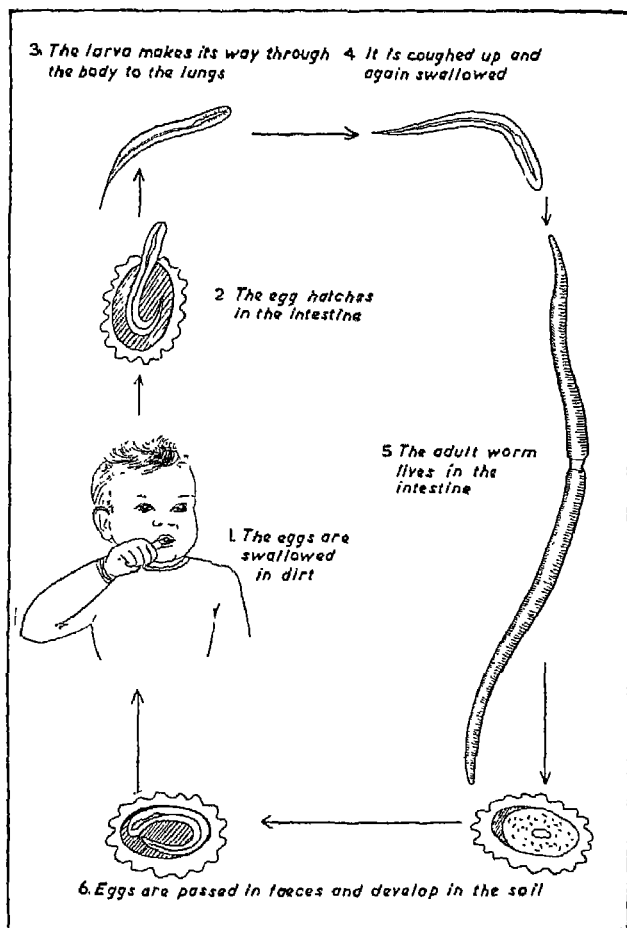


FIG. 11.—The roundworm goes through all the phases of its life-cycle in the human body.

intestinal parasite. It does not, however, produce very serious symptoms.

All of these parasites are relatively simple, lowly forms of animal life with a life-cycle which, although it requires two different hosts, is not particularly complicated. There are other forms of worm-like parasites which present an amazing example of adaptation. The liver fluke, which is very common in sheep, passes through some of the stages of its existence inside the body of the sheep, but it requires at least two other hosts for its complete life-cycle. From the sheep the mature eggs pass into the excreta and on damp ground hatch into an entirely different form which must reach pond water very soon, since the next stage of its development is in the body of a small water snail of a particular kind. Within this snail the liver fluke undergoes a further change, taking a form quite unlike either its parent or the intermediate free-swimming form which enters the snail's body. At this stage it is capable of dividing over and over again, producing yet another form of life which can continue within the snail for some months. Finally, it makes another metamorphosis into a small creature with a round head and a long thin tail, by means of which it swims through the water until it reaches the grass at the end of the pond; there it must wait until it is eaten by a sheep or other animal. From the stomach of the sheep the liver fluke enters the liver, and in about six weeks time it is a fully developed fluke about an inch long. The damage caused to the liver is often so great as to be fatal, but before the liver fluke destroys its host it will have produced very large numbers of eggs which will continue this astonishing example of adaptation to a parasitic existence.

That does not exhaust the list of parasites that infect the human intestines; but most of the others are to be found in tropical and sub-tropical zones only. They include single-cell protozoa, of which the amoeba, one of the lowest forms of single-cell life, causes the very distressing and difficult condition called amoebic dysentery. There are a number of these amoebae which can live in the human alimentary tract, and are called "entamoebae," from the Greek word *enteron*, meaning intestine; but it is one particular form, the *Entamoeba Histolytica*, which causes the disease. In the intestines it moves about searching for food, as do all other amoebae, but it can change into a cyst-like form which can survive outside the human body and so can be carried in food, or water, from one sufferer to a new victim.

We have already described the way in which the malaria parasite is conveyed by the mosquito and how it passes through two different stages of development in the human body and in that of the insect. Another disease conveyed by an insect, and due to a parasite living in the blood stream, is sleeping-sickness. It is the tsetse fly (Fig. 6) which conveys this disease, infecting human beings as well as other animals, particularly in the tropical parts of Africa. The parasite in this case is the trypanosome, a motile protozoon, which has a fin-like structure along its body and a slender whip-like tail (Fig. 12). It moves freely in the blood stream. As is suggested by the name of the disease it causes, it saps the energy of the human being who is infected by it. Here again the disease is best prevented by measures to destroy the tsetse fly, chiefly by destroying the type of jungle country which favours its breeding.

Another small parasite which infects the blood stream is the filaria, which also gets into the lymphatic channels of the body and, by blocking them, produces the condition known as elephantiasis. The name arises from the fact that when the tissue fluid is prevented, by the blockage of the lymphatic channel, from getting back to the blood stream, the part

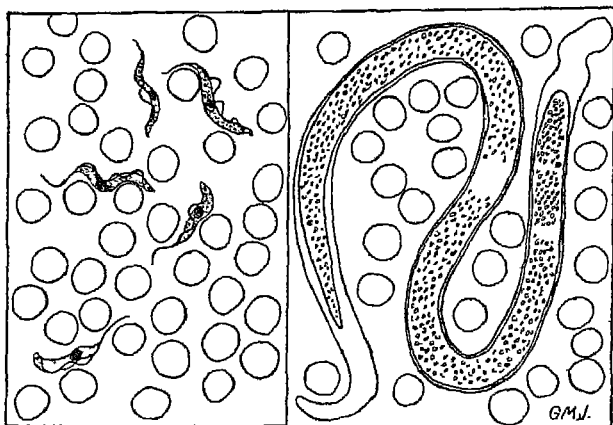


FIG. 12.—Trypanosomes and Filariæ are found in the blood stream.

infected (usually the leg) becomes enormously swollen and resembles the leg of an elephant. Different forms of this parasite show a peculiar periodicity in their habits and are to be found in the blood stream only at one time of the day (Fig. 12).

This brief description of a very varied group of enemies of mankind should also include a reference to those which attack the outer covering of the human body, the skin itself. The skin has a considerable

immunity to attacks, but certain fungi, of which ringworm is perhaps the most common example, do invade the skin. Ringworm is caused by a parasite which in its behaviour within the skin reminds us of the much larger fungus which produces the fairy ring of toadstools on grass. Some forms attack the hair, some the nails, and some the skin itself: all have a

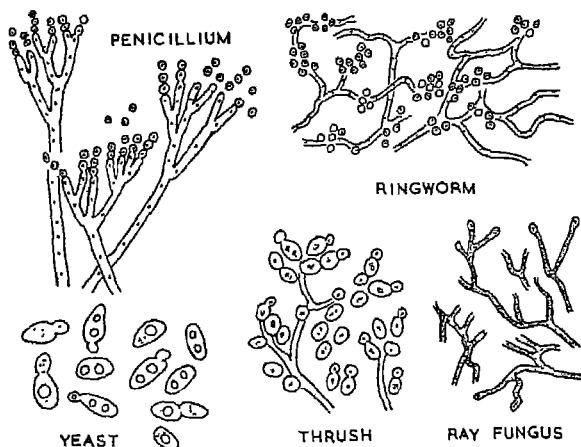


FIG. 13.—Some of the more common types of moulds and fungi.

considerable degree of selectivity for the particular part of the outer covering of the body in which they can grow. These fungi lie somewhere between the bacteria which we already described and the lower forms of plant life; they include forms such as the common yeast, which man uses for the production of alcoholic beverages, and the *Penicillium*, which is proving so helpful in attacking bacterial infection (Fig. 13).

There are also parasites which are really small animals and which burrow into the skin. Some of these are tropical. The most common is the small spider-like creature which produces scabies. This creature is the *Acarus Scabiei*, and it is about 1/80th of an inch long. It is the female which burrows into the surface layer of the skin in order to deposit her eggs. The irritation caused by the acarus leads to the popular name of the skin condition produced, "the itch." This creature passes very easily from one victim to another, especially when there is close contact. In recent years new drugs have been discovered which destroy the creature very rapidly.

For practically all these parasites man has discovered either means of treatment or means of prevention. The means of prevention are almost always based on a general improvement of the conditions in which human beings live. Whether we are dealing with a tropical parasite or an intestinal parasite familiar in our own country, the solution to the problem lies in interrupting the life-cycle of the parasite or of its insect carrier, or of improving general living conditions by cleanliness, by good sanitation, and by avoiding overcrowding and unhygienic habits. Science has practically triumphed in this field, but the methods it has worked out have not always been applied with the necessary vigour and expenditure of money on the part of those who are responsible for the health of the community.

CHAPTER X

STRUCTURE AND HEALTH

THE search for health is a search for the most nearly perfect physical structure and functioning of the human body. In the preceding chapters we have shown how, both by its own mechanism and by the assistance that science can give it, the human body has many ways of overcoming diseases caused by infective agents and parasites. There are, however, a large number of diseases and defects that may occur in the human body without, so far as we are aware, any action on the part of agents from outside. It will be realized that the development of the human body is an exceedingly complicated process, and it is not altogether surprising that things may sometimes go wrong.

Every human body begins as a single cell, from which, by a process of repeated and rapid division, the millions of cells of the adult body are provided. At the start of this process the cells that divide are all alike; but, as the process goes on, groups of special cells are set apart to develop in a variety of ways into the separate organs and tissues of the body. This development is not a straightforward process; in the course of its growth in the womb the foetus retraces to a considerable extent the evolutionary development through which the human race has reached its present state. That development includes fish-like stages in which gills are present, and there are therefore many

possibilities for developmental defects. In the first place, some of the cells may retain their primitive form and fail to fit into their proper position in the adult body. Instead of making healthy tissue they may produce a particular type of tumour growth which will show itself according to its nature at various times of life, often with fatal results. A further possible abnormality is that, although the cells may have become correctly differentiated, the organ they eventually form may be misplaced or incomplete. Occasionally one organ in an apparently normal human being is entirely missing or present only in a rudimentary form; examples have been found which cover almost every organ of the body. Thus it is no uncommon thing for a child to be born with one or other of the many bones of the body absent or represented only by a very small and incomplete structure.

It is worth noting that in these cases modern surgery has been able to produce some of its greatest miracles. A piece of bone may be taken from one part of a body and grafted on to another part, where it will grow, not in the shape of the first part but into the normal form of the bone which it replaces. This grafting of one living thing upon another has long been a recognized process in the case of trees and plants. It is now possible to take healthy living tissue from one person and transplant it to another. This is a comparatively common procedure in the case of severe burning of the skin. Sometimes it is possible to take small areas of the skin from a healthy part of the patient's skin and graft them on to the destroyed area, but occasionally it is necessary to take it from another person.

The skin is a comparatively plastic tissue, and the

skilful surgeon can do a great deal with it in repairing damage to such parts of the body as the face. Special kinds of graft are necessary, and by a variety of devices new ears, new noses, and even new lips, have been formed. This form of surgery has been of great importance during the war, and many men with terrible facial injuries have been restored to something approaching normal appearance. The skill and knowledge obtained under war-time conditions will be of immense value in dealing with similar injuries which are not altogether unknown under modern industrial conditions.

Most of the examples of grafting are concerned with the replacement of small parts of an organ such as the skin or a bone by quite small pieces of tissue. A rib has been used to reproduce a jawbone missing from birth, but the large organs still defy the surgeon's skill. From time to time our daily newspapers publish stories of girls who have by a surgical operation been converted into men, or *vice versa*. These are usually cases of congenital defects which arise from the complicated way in which the sex organs develop, and all that the surgeon does is to shape the tissues more definitely into one of the sexes.

A recent grafting triumph has been achieved in the case of the eye—a most delicate organ and one in which repair of injury is always difficult. When the clear part of the eye, the cornea, has been damaged by disease or injury, it may become so opaque that light cannot pass through it and sight is impossible. If the opaque matter could be removed and a clear cornea restored, vision would again become possible. This operation, as will easily be realized, is one of great difficulty, requiring the utmost care. It can of

course be attempted only when clear corneal material can be obtained from the eye of a blind person in whom the cornea itself is clear but sight has been lost for other reasons. It is not an operation very frequently attempted, but in recent years several successes have been obtained.

The completely successful functioning of the human body depends on the presence of all the organs necessary for health, but life can still go on even if certain organs are missing entirely. It is not an uncommon thing for an individual to go through life with only one kidney, which may increase in size and serve the body almost as efficiently as the usual two. Clearly, however, if disease attacks the kidney the chance of survival with only one is much less than with two.

Another abnormality, of which there are many interesting examples, is that an organ, instead of passing through those stages of development which represent the evolution of man's ancestors, may stop growing at some point in this evolutionary review. If this happens to a vital organ like the heart, it may leave a fatal defect. If it happens, as is not uncommon, in those developmental structures which represent the gills of the fish, it may produce minor defects such as small cysts, which can be dealt with by the surgeon. Some of the developmental errors that occur have little or no effect on life, among these being the condition in which the organs of the body are all placed on the wrong side. They are present and they function quite well, but are placed in positions opposite to those which we recognize as normal.

Mention of the heart reminds us that defects in this organ may produce severe and widespread changes in

other organs and indeed in the whole body. Everyone is familiar with the person who has heart disease and cannot live a normal, energetic life. Defects of circulation may interfere with the normal functions of any part of the anatomy, and by this interference lead to further defects.

It will be recalled that inside the heart there are a series of valves which control the flow of blood. Certain bacteria—strains of streptococci in particular—attack the valves of the heart and may cause so much damage that the valves cannot close and therefore cannot control the passage of the blood. Such disease usually begins as an acute feverish illness which is now successfully treated with Penicillin. It was at one time usually a chronic condition, and may still become so. In that case, because the flow of the blood is upset, secondary changes in the lungs and the liver and other organs are produced. The small blood vessels feeding the heart itself—the coronary arteries—are also frequently the seat of disease which causes the walls of the blood vessels to become harder and therefore less efficient, and sudden death is frequently caused by the blocking of these blood vessels.

This thickening and narrowing process may occur in any part of the circulation, and if it is sufficiently severe to deprive the organ of a full blood supply, it will lead to degenerative changes in the tissues. This is, of course, the process associated with old age, and it leads gradually to a decline in the function of the organ most affected. Those changes in function are of course related to the particular forms of structural change which occur.

One problem which affects both those of old age and those in industry is that of rheumatism. This is

a disease of many manifestations and of great economic importance. It accounts for a tremendous number of hours lost in industry, and its crippling effects mar the lives of millions in this country. It is not a straightforward disease with one cause, but is a complex in which germs such as the streptococcus, conditions of living generally, the housing of the individual and the conditions under which he or she works, all make a contribution. Treatment is therefore not by any single method, but by a combination of many. Massage, electricity, remedial exercises, vaccines and injections of gold, all play their part in restoring the rheumatic victim to health. People are too prone to disregard the first signs of rheumatism because it is so common among our population; but it is in the early stages that most can be done and at which it is important that everyone should seek medical advice.

In speaking of defects of development we should have mentioned that sometimes the process of growth seems to go a stage further than is normal, and people are born with a few extra organs. The most common of these are extra fingers and toes—which may or may not be inconvenient. If they are, the surgeon is usually able to deal with them. It is of particular interest, however, that this appearance of extra digits is hereditary and passes from one generation to another.

One of the most interesting things about the human body is the way in which its function as a whole is dependent on the presence of certain chemical substances which are produced within the body in certain small glands—the endocrine glands—which elaborate and pass into the blood stream secretions that are vital to life. These internal secretions, as they are

called, are in some ways the real controllers of the human race. They all interact together, and, although the amount of each of the internal secretions is exceedingly small, nevertheless in a normal person the amount of each appears to be kept under strict but very delicate control. It is by the internal secretions that such processes as those of growth, sexual development, the size and shape of the adult body, the appearance of hair, and even the mental outlook and temperament, are decided.

The work of the endocrine glands is so complex that we can do no more here than give a limited suggestion of how they function. Since we are concerned primarily with the defects that may arise in the human body, we shall consider this subject only from that point of view. The endocrine glands are, of course, subject to the development errors which we have just been describing, so that even quite early in life abnormalities may arise. One of the commonest of these is the presence of a tumour in the adrenal gland which, by exciting the other endocrine glands, may cause a child to be precocious mentally and physically. Such cases demonstrate very clearly that we are in fact what our endocrine glands make us.

The endocrine glands are subject also to infectious diseases and other injuries which may destroy or interfere with their function. The adrenal gland, which is often called the suprarenal gland because it lies just above the kidney, is occasionally infected by the tubercle bacillus, which destroys the tissue of the gland and produces a condition of ill-health and weakness which can easily be recognized as due to this cause. The adrenal gland is of particular interest to us, for it illustrates one of the advances that have been made by

science in elucidating the work of these glands. It is now known that the adrenals make a substance, called adrenalin, which passes into the blood particularly in times of stress such as fear or anger. We have now been able to isolate adrenalin in a pure form, and it can actually be manufactured artificially. We know, therefore, its complete story, and we are able to reproduce its effects experimentally. Its most important effect is on the blood vessels, which it causes to contract; it is therefore much used by doctors in stopping bleeding.

The gland which is most familiar to everyone is the thyroid, which lies in the neck, in front of and on both sides of the windpipe. This gland, if it is not the leading member of the endocrine team, is in some respects the chief controller of bodily activity, because it regulates the rate at which the body uses up its supply of foodstuffs. To maintain life we must utilize a certain minimum amount of food, and this minimum is greater or less than the average according to the way in which the thyroid gland acts. If it produces too much of its internal secretion, then all parts of the body work too fast, and we have the type of person who is thin and energetic. The acceleration may, of course, be within what we would regard as normal limits; but if it goes to excess we have a definite disease, in which the heart beats too quickly and the patient is in a very nervous state. A prominent symptom of this trouble is the way in which the eyes bulge, giving the disease its name of exophthalmic goitre.

The thyroid gland may, however, produce too little of its internal secretion, and in such a case we have the reverse effect. Everything in the body is

slowed up; food is stored instead of being utilized, and there is a tendency for the heart and the brain to go slow. The exact effect produced by this change depends on the stage of bodily development which has been reached before the thyroid gland ceases to function properly. If it occurs early in life, body and mind fail to develop, and the child will be a cretin of small stature and very deficient mentally. If, on the other hand, the disease occurs in adult life, the mental processes are again slowed up, the skin becomes rough and coarse, and in general the bodily functions are torpid.

Whatever the type of thyroid deficiency, we can safely claim that science has conquered it. The internal secretion of the thyroid has been isolated and its chemical formula is known. It can be manufactured and administered to those patients who are lacking in it, and in both the child and the adult it produces a remarkable return to normal health. In such cases, however, the gland itself does not return to normal, and the body can be maintained only by continuously supplementing the deficient internal secretion by the artificial preparation.

Where the thyroid is over-active, the surgeon is able to remove a part of the gland so that the amount of secretion getting into the blood is reduced to something like the normal level. In recent years, however, a chemical substance, thiouracil, has been discovered which interferes with the excessive secretion of the thyroid gland and reduces it almost as if a part of the gland had been removed. In cases which are diagnosed early and treated efficiently this method supersedes the surgical operation, which was always attended with some danger and left somewhat promi-

nent scars. Thiouracil is not without some danger, for it may adversely affect other organs; and it has not yet been used for a sufficient number of years for us to be quite certain whether its effect goes on after the patient ceases to take the drug, or whether it has to be continued during the whole of the life of the patient. Its mode of action is not quite clear, but it appears to interfere with the way in which the thyroid gland uses iodine. This element is present in our food in small quantities and forms an essential part of the thyroxin, as the thyroid gland secretion is called. It is interesting to note that there are certain areas in the world where the amount of iodine in the soil is so small that very little is obtained in food or in the water; in such areas goitres may be frequent and children who fail to reach the normal stature and development are not uncommon.

Science has had a very difficult task in working out the functions of these glands, but space does not permit us to tell the story in full. It has always been realized that human beings differ widely, both in physical and in mental attributes, but it was not until the first of the glands of internal secretion was recognized that it was demonstrated why these differences in human beings should occur. Some of the glands are exceedingly small, and all of them produce their secretion in very small amounts, so that medical science has had to devise all kinds of new methods in order to trace the function of each of them. The pancreas gland may be taken as an example both of the difficulty of discovery and of the triumph finally won by medical research.

The pancreas gland is that known as the sweetbread. Many years ago it was recognized as the

gland which pours through its duct into the stomach the juices necessary for digestion. We also learned that, while certain other organs of the body could be removed without fatal result, the pancreas could not be removed from an animal without causing death. The mode of death, however, did not resemble that due to the absence of the digestive juices; it was of an entirely different kind, and close study of animals revealed that removal of the pancreas produced a disease very similar to the condition known in human beings as diabetes. In this disease, as probably every one knows to-day, the patient has an unusual thirst and an abnormal desire for sugar; another notable symptom is the presence of sugar in the urine. Normally there is no sugar in the urine, and its appearance is usually regarded as a sign of diabetes, although this is not invariably the case.

The symptoms that develop in an animal from which the pancreas gland has been experimentally removed are those of thirst and a desire for sugar, as in the case of humans. Clearly these effects could not be due to the ordinary secretion of the pancreas, and they were finally traced to the presence, mixed up with all the cells of the pancreas gland, of another type of tissue which, we now know, forms one of the endocrine glands. The highly specialized cells of this gland occur in the pancreas in small groups, known as the Islets of Langerhans (Fig. 14).

Research in this field was complicated by the fact that the islet cells could not be separated by any method from the ordinary cells of the pancreas. Further, the isolation of the secretion of the endocrine portion of the gland proved very difficult because the secretion was destroyed by the digestive juices. It

had been observed, however, that if the duct of the pancreas gland got blocked for a long time, the pancreatic tissue died but the islet cells remained unharmed. This effect was produced experimentally in dogs, and, when the pancreas in which the digestive juices had thus been abolished was removed, it was

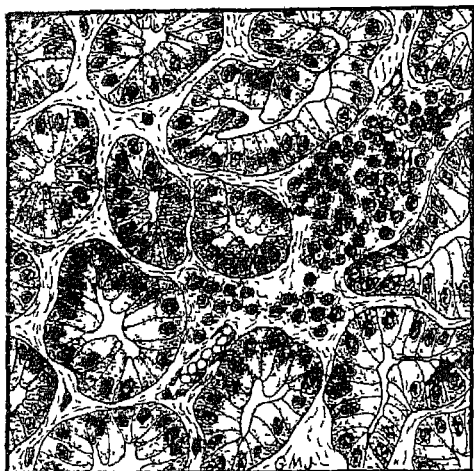


FIG. 14.—The Pancreas gland, showing the insulin-secreting cells and the more abundant cells secreting digestive fluid.

found possible to isolate the secretion of the islets. This secretion was then given the name of insulin. Further experiments proved that it was the removal of this substance from an animal which produced the symptoms which had for centuries been recognized as diabetes. The triumph of science was complete when it was found that by an injection of insulin the symptoms could be abolished.

Insulin is now available in a chemically pure form and is in every-day use by diabetics all over the world. Its power to control the symptoms of diabetes is universally recognized, and it has certainly saved a very large number of lives. It is not yet possible, however, to reproduce precisely the delicate control which the normal islet cells have over the utilization of sugar within the body. This control is, in the normal body, so sensitive that the amount of sugar present in the blood is kept at a very constant level. Any excess from newly eaten food is stored by the liver, and any deficiency in the muscles, which are constantly using up sugar, is made up by sugar leaving the liver. This mechanism is all controlled by the amount of insulin present in the blood stream, but the delicacy of the balance between the amount of insulin and the action of the liver and of the tissues is almost beyond comprehension. Science has defeated death due to the lack of natural insulin, but it has not yet found an absolutely correct method of replacing it in the body. Forms of insulin are, however, now available which, when injected under the skin, pass into the blood very slowly and so come very near to producing the normal state of affairs. No method is known of restoring the diseased pancreas gland to normal activity, but the methods of replacing the insulin now available have greatly eased the life of the diabetic and may lead to the production of a new product which will be almost as efficient as the natural secretion of the islet cells.

Among the other endocrine glands there are two which are chiefly concerned with the human skeleton. The first of these, the pituitary gland, lies at the base of the brain, inside the skull, and it has so many inter-

relations with the other endocrine glands that it is very often regarded as the governor of all the other glands. It is a small gland about the size of a hazel nut, and its chief function is to control the growth of the bones. Occasionally it overacts and produces a disease called acromegaly, in which the skull is very much thicker than usual, the jawbone increases in length, leading to a particularly easily recognized type of face, and the hands and feet become very large. If the pituitary overacts in this way during adolescence, when the bones are most actively growing, the result may be a person of much more than average height.

Bones can be formed only if the element calcium is present in sufficient quantities. Normally the amount of calcium in the blood stream remains very steady. Here the adjustment is under the control of four glands, each of which is a little more than a pin-head in size, called the parathyroids. They take their names from the fact that they lie close to the thyroid gland, in the neck. So long as they are present and produce their secretion in the right amount, bones are formed of normal hardness because they contain the proper amount of calcium. Occasionally, however, too much secretion is produced by the parathyroids, usually because one of them has grown into a small tumour; the body is then unable to retain calcium in sufficient amount. The chemical analysis of the blood will show that more than the normal amount of calcium is circulating and more is passing out of the body.

As a result of this condition the calcium of the already formed bone begins to decrease, the bones become more and more brittle and liable to sudden

and repeated fractures. In one famous case nearly every bone in the arms, legs, and chest had been broken before the true nature of the trouble was recognized. A skilful surgeon removed a small tumour of one of the parathyroid glands and at once the patient's body began to absorb and retain calcium. Bones became hard again and the fractures joined up in good, sound bone.

An exceedingly complicated part of the story of the endocrine glands concerns those connected with reproduction. Just as the insulin-producing gland is mixed up in the pancreas, so the reproductive glands contain cells which produce an internal secretion. It is the activity of these cells which controls the normal development of puberty and causes the appearance of the secondary sexual characters. In the female the reproductive glands have a multiplicity of secretions which science is still struggling to separate. These secretions control the whole process of reproduction, and on their presence at the right time and in the right amount depends the occurrence of normal conception and of the normal development of the unborn child. The disturbances that occur in the life of a woman around middle age are due to a faulty balance in the secretion and to an absolute diminution in their amount. The chemist has in recent years elaborated many substances which, if not precisely those of the ovaries, are at least related to them and are able to a very large extent to relieve the symptoms of the climacteric in most women.

Sex abnormalities of varying degrees are fairly common, and these are in most cases related to variations in the internal secretions of the reproductive organ. It is hoped that when all the secretions have

been identified and can be prepared artificially we shall have at our command weapons which will enable us to control the development to full maturity of both sexes. It is, however, quite impossible to give any indication of the real complexity of this problem. The recognition of the part played by the internal secretions of the reproductive glands has provoked great interest, not only in the medical profession but also among the lay public. Since the ultimate control of growth depends on these secretions, it is a fairly obvious idea that by their use the body might be kept young and active. From this there has grown up a considerable belief in the rejuvenating power of preparations made from sex glands. So far, however, the action of these is uncertain and most of the claims made have not been substantiated.

On the other hand, the chemists who are busy with these investigations have discovered certain potential dangers. Chemically it appears that one of the sex hormones is closely linked to substances derived from tar, which is known to have the power of causing cancer in experimental animals. The particular hormone which is already fairly widely used is known as oestrin; and while at the moment it has not been shown that this substance has any effect on the production of cancer in human beings, its chemical relation causes it to be viewed with considerable suspicion. The revelation that substances having such wide and varied effects on the human body are chemically related indicates something of the complexity of the problems which modern scientific medicine attacks.

The substance oestrin is also chemically related to another group of substances which play a very im-

portant part in the machinery of the human body, notably to the chemical group which includes vitamin D. There is no need at the present day to describe what vitamins are; everyone must be by this time aware of the important part played by these strange chemical substances without which a normal human body cannot develop and cannot continue in health. The hormones or internal secretions which we have already described are elaborated inside the body, and by their interaction control most of the normal processes of the human organs. These normal processes, however, depend also on the presence of other chemical substances which the body cannot itself make; these are now spoken of as the vitamins.

As they have been discovered, the vitamins have been distinguished, not by names, but by letters of the alphabet. Vitamin A is now known in pure form and its functions are being carefully worked out. Vitamin B, on the other hand, has been found to consist of a large number of chemical substances which could not at first be isolated completely one from another. The absence of the vitamin B complex produces very definite diseases. In prisoner-of-war camps, especially in the Far East during recent war years, very large numbers of people suffered from the disease beriberi because their diet contained no vitamin B. A very common and fruitful source of vitamin B is yeast, but it occurs naturally in certain vegetables and in part of the seeds we use as cereals. Vitamin E has not yet been completely identified either as to its composition or its function, but it plays some part in regulating fertility and has been used with success in treating certain cases of repeated abortion. Vitamin C has been shown to be a comparatively simple

organic substance, occurring in large quantities in fruits such as the orange and lemon.

It is one of the romances of modern chemical advancement that for a long time it was recognized that the taking of the juice of such fruits prevented the development of the disease known as scurvy, which at one time was very prevalent and very dangerous. Scurvy has almost entirely disappeared from the civilized world, but occasional cases still occur in our large cities. A serious case which occurred in an unemployed man in London during 1935 gave research workers one of their earliest opportunities to observe the exact amount of vitamin C, or ascorbic acid, which the body needs. The body requires enough ascorbic acid in the diet to keep it saturated with this substance, but when more than that amount is present the excess is excreted in the urine. This has enabled a very simple test for vitamin C deficiency to be worked out; the body which already has enough will excrete an excess given by the mouth, while the person suffering from deficiency, and therefore a potential case of scurvy, will not excrete any that is given until the body is fully saturated again.

Vitamin D is familiar to everyone in the form of cod-liver oil and in the form of oil from the liver of other fish. It has also been isolated in pure chemical form and can be manufactured artificially. If the very small quantities that are usually required by the body are absent, rickets will occur. It was this disease which at one time produced the very large number of "bow-legs" and other bone deformities that occurred in young children. The amount of vitamin D required to prevent the occurrence of rickets is very small indeed, and the person taking

the ordinary mixed diet does not, as a rule, need any addition in artificial form. Rickets was at one time considered to be caused by the overcrowding, insanitary surroundings, and lack of sunshine with which it was so often associated. This was undoubtedly the case, for in these conditions even the small amount needed was often absent from the diet, and the lack of sunshine aggravated the condition, because the formation of natural vitamin D is related to the action of sunshine on the skin. It is a sharp commentary on modern affairs that, while science has conquered scurvy and rickets, it has not yet overcome the other forces in the shape of bad economic distribution which, by preventing people from obtaining a diet containing enough of these precious chemical substances, leads to the continuous existence of crippling diseases that should long ago have vanished.

Lack of the necessary amount of vitamins in a section of the population is only part of the greater problem of the adequate nutrition of our industrial population. There have always been a certain number of people who have maintained that a large portion of the working-class of this and other countries are unable to obtain an adequate diet. Just before the war evidence was accumulating that millions of the population were unable to purchase anything like the amount or the quality of the food which science shows is necessary for health.

One of the most important of these statements—that of Sir John Boyd Orr in 1938—declared that at least four and a half million people in this country were unable to obtain a diet which contained adequate amounts of the substances necessary for health. There appears to be no question that at least 10

millions of our population in the years before 1939 received a weekly diet far below the minimum essential for good health. Sir John Boyd Orr concluded that "as income increases, disease and death-rate decrease, children grow more rapidly, adult stature is greater, and the general health and physique improve." It is the aim of medical science to ensure that every person in the community receives a diet which will permit of the optimum rate of growth and the maintenance of perfect health. Until that has been achieved, at whatever economic cost, much of the work that is done and many of the discoveries that are made by research workers will fail to have the effect they might have in ridding us of disease.

CHAPTER XI

HEALTHY MINDS AND HEALTHY BODIES

It has long been a commonplace that a healthy body is of little value if it is not accompanied by a healthy mind. This obvious truism has been very difficult to translate into practical terms, for while the physiologist can come very close to a definition of a healthy body there has been no such agreement as to what we can expect of a healthy mind, and no certain method of assessing the mind in such terms. Indeed, there is no clarity about the definition of the word "mind." People generally have a very vague notion of what they mean by the term, and their vague notion is complicated by a great number of superstitions about the mind—in particular by the attempt to regard the mind as something apart from the body.

Modern medical knowledge has made it increasingly clear that the mind depends, as do all other things connected with living things, on physical changes within physical organs. In other words, it is impossible to divorce the mind from the brain and the nervous system generally. But even recognition of this close relationship does not make our definition of a healthy mind any easier. The brain can be to all practical purposes—and to all our known tests—normal and healthy, but it does not necessarily follow that the mind—the thoughts, ideas, and ideals that it contains—will be healthy either for the in-

dividual or for the community in which he or she lives.

On the other hand, we have at least advanced towards a new conception of the way in which departures from the average civilized functioning of the mind should be regarded. We search for the cause of those departures in abnormalities that can be tracked down, checked, and very often corrected. Those abnormalities may be defects of thought, of behaviour, of experience, or they may be abnormalities of the physical structure of the brain.

No more striking example can be given than the change in character, in mental processes, and in nervous reactions, that follow upon certain diseases. The individual whose temperament and behaviour suddenly take on unusual forms, rendering him unhealthy in relation to the rest of the community, will cause his doctor to think at once of a disease such as syphilis. Syphilis, we know, is caused by a pathological organism, the spirochaete, which may invade any organ of the body, but at a certain stage is very prone to attack the central nervous system and especially the brain. The pathological changes which it causes there lead to abnormalities in the mental processes.

An equally striking example is that of encephalitis lethargica, or sleepy-sickness, which occurs as an acute infection of the brain by one of a group of living things yet to be described—the viruses. In the acute stage the symptoms mainly observed are neurological—that is to say, clearly and definably due to changes in the nerves themselves. From these acute attacks the patient usually recovers, and he may continue through life with very little to reveal the

previous disease. Some cases, however, go on to a phase in which the outstanding feature is a change in behaviour. The sufferer becomes exceedingly irritable and refuses to conform to the ordinary usages of society, being often violent and usually remaining at a state of mental development very much lower than is normal for his actual age. At a later stage general deterioration of the brain may ensue.

An operation which has been performed recently on such cases demonstrates beyond all doubt the dependence of the mind and of thought processes upon the actual physical condition and reactions of the brain. By a very clever surgical process, known as pre-frontal leucotomy, certain fibres of the brain are cut through. When the patient recovers from the operation and the nerve tissue has healed, the whole behaviour, attitude, and mental development changes; they become quiet, and although it may never be possible to bring their mental development up to the level appropriate to their physical age, they become educable and can be allowed to mix normally in the ordinary social circle.

The stage we have reached in regard to nervous and mental diseases is that of discovering methods of more exact diagnosis. In order to meet this need, increasing attention has to be given to the very earliest signs of mental instability. One of the features of medical science during the second World War was the development of new techniques for dealing with early mental disorder; the results obtained from the prompt treatment of soldiers who under the stress of battle were developing mental instabilities have been really tremendous. Psychology has advanced at a great rate, and, while it is not always an exact science,

it is evolving methods that enable many who would otherwise have been doomed to mental decay to be restored to comparative health.

Another interesting recent development has been the study of electrical impulses within the brain. By means of the encephalograph minute electrical impulses darting from one part of the brain to another can be traced and recorded on a chart. There seems no doubt that the pattern obtained is an indication of the amount and character of nervous and psychological action taking place within the brain; and for the normal person the pattern is already fairly well known. Many of the various forms of psychological instability are reflected in the tracing obtained by this method. The public hear of this mainly in connection with trials for murder, but the method has much wider applications.

It is clear that the field of psychology must always be of the greatest importance in regard to those mental conditions that can be recognized as abnormal. That is, however, not its only value. It is now known that the psychological study of the normal individual can lead to many conclusions as to his or her capabilities and may enable an assessment to be made as to the vocational possibilities of any particular individual. This technique has had its most widespread development in the armed forces, where the selection, for example, of personnel for different duties in the Royal Air Force was largely controlled by psychological study. In peace-time it can be applied in industry and in occupational life generally, where it should be possible to select people for different jobs in such a way that the square peg in the round hole becomes a rarity. In this way modern psychiatry

and applied psychology can assist adults in maintaining as great a degree of health in their minds as they can, by other methods, maintain in the body. With children, however, the method may have even wider repercussions. Psychological problems begin to arise at a very early age, and the application of modern methods to the child and to the guidance of parents in regard to their children is not yet fully developed.

The greatest problem, however, is that already mentioned of deciding what is a healthy mind, so that methods may be elaborated for its preservation. It is relatively easy to assess the intelligence-level and the range of intellectual attainments, but it is exceedingly difficult to guarantee that these are used for healthy thoughts. Our thought processes affect our whole life and the lives of those around us, and it is clear that one of man's later developments must be the recognition of the basis upon which the mind acts, the inculcation of rational methods of thought, and the greatest possible effort to control the processes which to-day prevent many from achieving mental health.

CHAPTER XII

INDUSTRIAL DISEASE

THERE are many diseases and defects which arise from the way in which modern man lives and from some of the activities in which he engages. The types of disease we have already described cannot be said to arise directly from such activities, although in the case of bacterial and parasitic conditions man's way of living and lack of knowledge often encourage or perpetuate the disease. The errors and defects that arise in the various stages of growth are largely outside man's power even to prevent, although a number are so clearly hereditary that the civilization of the future may attempt to avoid them by restrictions on the marriage of those known to have such defects.

It is unnecessary to remind the reader that a great volume of incapacity and a very large number of deaths are caused each year by accidents of one kind and another. By the very meaning of the word, accidents should be entirely unforeseen and unexpected, but on analysis it is astonishing how large a proportion of cases do not quite fall within this class. There are many so-called accidents in the home, in the street, and in the factory, which are so clearly related to our mode of living that science has been called in to suggest methods by which they may be prevented.

It is in industrial processes involving the use of heavy or rapidly moving machinery that we find the

greatest danger. In the early development of modern industry these dangers were regarded as inevitable, and those who suffered as a result of them were considered merely to have been unlucky. That attitude has now been changed, and by a variety of rules and regulations many safeguards have been introduced into industrial processes. Factories are subject to expert examination, and there are many devices and regulations for the prevention of accidents. It is impossible to describe these in detail, but rapidly moving machinery must be protected one way or another so that hands and clothing cannot be caught in it, and the worker himself is given detailed instructions to safeguard him from any dangerous machine he has to handle.

Different industries have, of course, their own particular types of accidents. One of the most dangerous of all industries is that of coal-mining. Every large mining disaster forces us to realize how hazardous is the business of producing coal, but few people remember that, apart from disasters in which even hundreds may be killed by one explosion, there are deaths and injuries to many miners every day. The prevention of these accidents is a complex problem, but solutions of most of the difficulties have been worked out. They include such things as better lighting at the coal face, better methods of building up the walls of the mines, and the provision of better tracks for the underground railways. It is anticipated that increased mechanization within the mines, which is part of the design of the nationalization scheme, will assist in reducing such accidents. The important thing in the mines to-day is that the measures which have been developed for avoiding accidents should be enforced.

Apart from accidents there are diseases related to mining. One of these—miner's nystagmus—was for many years the subject of great controversy. As the miner has to work in surroundings that absorb practically all the available light, his eyes are subjected to an abnormal strain which may cause a breakdown in vision and in general health.

Another disease associated with mining is silicosis; it occurs also in other industries. Dangerous in itself, it increases the likelihood of pulmonary tuberculosis, so that those who once contract it run a double risk. It is due to the inhalation of small particles of silica, which is the chief constituent of many rocks and is therefore present in the dust produced by mining operations.

One of the great difficulties in connection with industrial diseases is well illustrated by the history of silicosis. Many years passed before it was officially recognized as an industrial disease and before arrangements were made for compensating those who had contracted it. In many instances the disease develops very slowly, and usually by the time it is recognized so much damage has been done that recovery is impossible. Silica is a danger not only in mining but in those industries preparing and using stone, and where sandstone is used for grinding metals. There is only one method of preventing this disease—namely, to ensure that no silica gets into the lungs. This is not always an easy process, for so long as substances containing silica are manipulated in a dry state there is every possibility of some particles being inhaled at every respiration. Closely related to silicosis, and causing a very similar condition, is asbestosis, which has been recognized only in quite recent years.

Another substance which frequently gives rise to disease is lead, which is fairly widely used in industry not only as metal but in equally dangerous forms as white lead in the making of paint and as glazes for certain kinds of pottery. Lead poisoning affects different parts of the body and is usually recognized from the changes it produces in the red blood cells. At one time it was a very serious and widespread disease among those coming in contact with lead in industry, but measures which have been adopted have diminished it to a considerable extent. Many substitutes have been found for lead, and its uses are now much less important than formerly.

When a material or process causes disease or death rapidly, it is relatively easy to recognize. There are, however, some conditions that take many years to develop. For example, there is the case of cancer of the skin, which may be caused by the constant application of small quantities of certain chemicals. The most common of these is the cancer produced by the use of mineral oils for lubrication, particularly in spinning mills; it is often referred to as "mule-spinner's cancer." In such cases the oil used for lubricating the machine was constantly being splashed on to the clothing, and after a period of years—which might be as long as twenty—a cancer might develop where the oil had been deposited. It is now certain that this effect is not due to the oil as a whole, but to one particular chemical substance which is present in the oil; and by substituting a vegetable oil from which this "carcinogenic" substance is absent the danger can be removed.

There is also the case of workers using aniline dyes, who sometimes develop cancer of the bladder, which

is apparently due to one of the chemical components of the dye-stuff employed. There are, of course, other dangers from these dye-stuffs, and some of them produce very bad effects on the skin.

The skin, it will be clear, must suffer frequently from irritation by industrial chemicals. Occupational dermatitis is now a very clearly recognized disease, and more than thirty different forms have been listed. There are at least forty chemicals in fairly common use, ranging from soap and soda to those used in making high explosives and poison-gas, which may produce such a skin condition.

One of the relatively modern examples of occupational dermatitis illustrates how difficult it is always to foresee the danger. As everyone knows, the heads of the flower "pyrethrum" are dried and powdered and used in insect powder. The amount of pyrethrum powders used, both in the home and in the garden, is enormous, and most of the flowers came originally from Japan. In Japan the flowers are at a suitable stage for picking only during a relatively short period not exceeding two months; the workers concerned did not seem to suffer any inconvenience. Some years ago, however, this industry was introduced into Kenya, where the different climate allows a flowering season of ten months in the year, with the result that those engaged in the picking of the flowers are exposed for a very long period to the effects of pyrethrum powder. In many cases a severe dermatitis developed.

Mention of the pyrethrum danger recalls that agriculture as well as the factory has its occupational risks. There are quite a large number of plants which cause dermatitis; even such ordinary plants as the

daffodil have been shown to be capable of causing a skin eruption in susceptible people.

Other agricultural workers run dangers from germs which infect sheep and cattle. The dairy farmer may, for example, contract the fever known as undulant fever in the human being, and as abortion fever in the case of cows. The germ causing this disease is conveyed in the milk, but may also infect human beings by direct contact. Although a long and debilitating disease, it is rarely fatal. It is now known also that "louping ill," a disease of sheep, may occasionally infect human beings, although most shepherds appear to acquire an early and high degree of immunity to it.

The subject of industrial disease is, however, too vast to be treated in full detail in this short book. Every day new substances are being produced and new uses are being found for previously known chemicals, and many are finding their way into articles in everyday use. The plastics and industrial solvents belong to this class and are too numerous to mention. Wherever a chemical substance is new or unusual there is a definite possibility of danger to those using it. It is quite clear that industry should be compelled to carry out all possible tests on such substances in order to ensure that nothing dangerous to human life or health comes into popular use or production until we are as certain as we can be that it is quite safe for human beings.

CHAPTER XII

INVISIBLE ENEMIES: VIRUSES

It was a great step forward for medical science when the bacterial theory of disease was first clearly demonstrated. At one step much that had been obscure in the causation of disease became clear. More important still, it became possible to visualize methods of tackling not merely the symptoms produced by a disease, as had been the case in the past, but the actual cause of the disease itself. The work of bacteriology had not gone very far before it became clear that there were a group of diseases which by their symptoms and general behaviour appeared to be infections, but in which no germ could be discovered or demonstrated.

From their effects on the patient most of these diseases could be classified as fevers or infectious diseases. In some cases germs were actually found to be present fairly constantly, and they were thought to be the true cause of the disease. Influenza is one example, for a small Gram-negative bacillus with very well recognized characteristics is almost always found in the nose and throat of sufferers. This microbe was in fact called the *Bacillus Influenzae*, and we have retained the name here; but the third postulate of Koch could not be proven, since the introduction of these germs into animals and man failed to reproduce the disease. Most of the diseases in this group, however, had no associated germ, and ultimately it was realized that, while clearly an infectious agency

was at work, that agency must be so minute as to be beyond our ordinary means of detection. Further, although the agency was apparently capable of enormously rapid growth in the human body—as is witnessed by the rapid spread of influenza—under ordinary laboratory conditions they were probably capable of only very small growth. In the case of influenza it has now been clearly demonstrated that the true cause is an agent of very small size known as a virus. It is the virus which begins the disease and is responsible for the characteristic symptoms; the *B. Influenzae* and other germs merely take advantage of the state of the body caused by the virus and in a secondary fashion attack the tissues.

It will be recalled that in order to see the ordinary germ we require a microscope of considerable magnifying power. Before the image of any object can be so magnified, even in the finest microscope, the object itself must be of such a size as to interfere with light waves, which we know are of definite lengths. An agent or object which is less than the smallest size that can interfere with any of the light waves cannot be seen by the microscope and is therefore spoken of as “ultra-microscopic.” The properties of viruses have, therefore, to be deduced in other ways, which we shall describe in a moment. In recent years, however, developments in other scientific fields have enabled new types of microscope to be produced in which waves shorter than those of ordinary light—e.g., ultra-violet rays—are used in order to produce images that can be photographed or rendered visible by indirect methods. The electronic microscope, using electrical impulses much shorter in wavelength than those of light, is now being used in the study of the viruses, and

there can no longer be the slightest doubt that they actually do exist. Magnifications of a half-million times have already been achieved, and some of the photographs reveal not only the size and shape of viruses but begin to clear up many other points about them. It is of interest to note in passing that some of these photographs taken with the electronic microscope reveal an internal structure in bacteria which by all other methods of staining had appeared to be entirely amorphous.

One of the best ways in which to demonstrate the existence of viruses is, of course, to pass them to other animals and observe whether the same disease is produced or not. We now know a number of virus diseases which can be easily and certainly recognized in the usual experimental animals. Material from a human case of disease thought to be virus in origin can be shown to produce recognizable effects in an animal to which such material is conveyed.

At one time it was objected that the transfer of material from one animal to another meant that other agents, chemical or bacterial, might be passed on, and might in fact be responsible for the effects which were being laid at the door of the virus. This led to experiments designed to filter off the viruses from all other objects of larger size. Filters can be made of materials of such a nature that the size of the particles which will pass through them is fairly accurately known. That is to say, all particles above a certain size will be retained by the filter, and those below that size will pass through it. In this way most viruses can be separated from most other elements, and they are therefore frequently spoken of as "filterable" as well as ultra-microscopic.

In passing it may be mentioned that by means of filtration all bacteria can be removed from the medium in which they have been growing. A porcelain filter is frequently used in bacteriological work, to separate germs which have been growing in a liquid medium from the toxin which they have produced in that medium. For certain bacteriological processes this is the best method of sterilization, since it does not involve heat or chemical action which might interfere with the toxin it was hoped to separate from the medium.

As mentioned earlier, it has been regarded as essential in the case of bacterial disease that the organism suspected to be present must be grown artificially before it can be definitely blamed for the disease. Most of the germs that we have described have their own way of growing and reproducing. They produce definite appearances in ordinary culture media. But in the case of the viruses this step in the proof that they cause disease is exceedingly difficult. A large-sized germ which grows in a fairly large colony can be seen on the surface of a solid culture medium. Up to the present no virus has been discovered which produces such a recognizable effect. Some evidence has been collected that viruses do multiply under artificial conditions, but the evidence is of a very technical kind and cannot be simply demonstrated as in the case of the larger bacteria.

Another difficulty is that the viruses do not appear to use the same foodstuff as the ordinary germ, so that such a simple demonstration as the production of gas from sugar (which is a feature of many of the common bacilli) is not at our disposal for testing the way in which viruses use chemical substances as food.

The most rapid growth of viruses appears to be in media in which a small piece of living tissue is present; in other words, they grow in close association with the animal body. This very fact introduces great difficulties in determining the exact way in which the virus lives.

As we have said, however, there are many virus diseases that are clearly of an infectious nature. One of the first to be investigated was rabies, at one time common among dogs all over the inhabited world and frequently appearing in human beings bitten by animals suffering from the infection. No one has any doubt that rabies is infective. It was because rabies was so clearly an infection that Pasteur made it one of the first diseases he investigated. In this he scored probably his greatest triumph, for although causative agents could not be found, and although the idea of a virus had not then been elaborated, Pasteur was able to develop a method of treatment which is still carried out and which corresponds very closely to methods used in diseases which we now know to be bacterial in origin.

Another disease which we can show to be due to a virus is distemper, a very common and highly infectious disease among dogs, particularly when they live in close quarters. This disease attracted an immense amount of interest, and the search for the infectious agent proved exceedingly difficult because no other animal appeared to be susceptible to the disease. It was only after all the usual test-animals had been tried that it was discovered that the ferret is highly susceptible to distemper; from this point it became relatively easy, not only to demonstrate that the cause of distemper is a filterable virus, but also to

produce from the infected ferret material which, when injected into dogs, conferred a considerable degree of immunity. This production of immunity to a virus disease is, of course, an important point in relating these agents to the ordinary bacteria.

We have seen that most bacteria, when they cause infection in the animal body, also provoke a reaction on the part of the tissues to develop anti-substances which destroy the invading germs and their poison and may also produce a lasting resistance to the disease. The same principle applies to most viruses, and it was first demonstrated in the case of anti-smallpox vaccination. Many of the more common virus diseases produce so much reaction that second attacks are uncommon, but it is unfortunate that this lasting immunity is not a universal feature of virus disease, since it appears that the common cold belongs to this group. Methods of using the antibodies produced by viruses in one animal for the treatment of other sufferers—as in the case of anti-diphtheria toxin, which was described earlier—are not yet fully developed. In a condition such as measles there is some evidence that the blood of any person who has once had the disease contains antibodies which remain throughout life. In the case of a child known to be infected a small injection of blood from the mother may contain sufficient antidote to assist recovery if not entirely to abort the attack of this very common disease. Quite a number of viruses appear to have particular affinity for the nervous system; both encephalitis lethargica (or sleepy-sickness) and infantile paralysis are due to virus infections. In both cases there is an acute feverish illness in which the nerve cells are destroyed.

Viruses, like bacteria, are conveyed from one victim to the other in a variety of ways. Those of the commoner infantile infections, the common cold, smallpox, and so on, are conveyed directly from one victim to the other. Rabies, as we have seen, is usually conveyed by the bite of a dog. It can, however, be conveyed in other ways, and a few years ago a most interesting discovery was made on the Island of Trinidad, where certain cases of an unusual nervous disease had been occurring. It was demonstrated that this was due to the virus of rabies, which on that island had infected large numbers of cattle, from which it was conveyed to man by a vampire bat.

Insects also carry viruses. One form of mosquito is responsible for the spread of yellow fever, a disease which baffled scientific investigators for many years because no animal was known in which the disease could be reproduced. When it was finally decided that the evidence pointed to a *virus infection* conveyed by a mosquito, the only way to prove it was with human beings. The full story of the investigations makes fascinating reading. In a series of tests the experimenters proved that normal people could live with those who had the disease, or could even be close to those who had died from the disease, without contracting it, provided that all mosquitoes were excluded. They then exposed themselves to the bites of mosquitoes which had come from those already ill with yellow fever, and at once they became infected with the disease. This proof enabled the work of freeing yellow fever areas in the tropics from the disease to be carried out by attacking and destroying the mosquito responsible for its spread.

The work on virus diseases is only beginning. We

do not know yet all the diseases that are caused by these minute agents. There is a possibility that in a mysterious agent known as the bacteriophage we have something in the nature of a filterable virus which attacks and destroys other bacteria. As yet, no success has been attained in developing a chemical substance that will destroy viruses as Penicillin or the sulpha drugs destroy ordinary bacteria. This is probably the field in which the next great advance may be made, but it is one in which the difficulties arising from the very nature of the agent to be destroyed appear almost insurmountable. However, since they have the attributes of living agents, they are susceptible to harmful substances, and the great search in the medical world to-day is to find a substance that will attack and rid mankind of those invisible germs which cause so much disease and death.

CHAPTER XIV

CANCER

As the scientist probes into the nature of the virus and the bacteriophage, he enters the field in which the physical, molecular, and atomic properties of the agents with which he is dealing become more important than their chemical composition. Indeed, the most recent work touches on the boundary between those things which we readily recognize as living, and those which we regard as non-living in the usual sense of the term.

It becomes increasingly clear that the whole structure of man is based on physico-chemical balances of great complexity. The whole process that goes on within living organisms, even within a single cell, is not only exceedingly complicated but it can be upset and sometimes given quite dangerous properties by a great variety of agents. In the case of cancer, which we have now to discuss, it appears that we are dealing with one of the strangest of phenomena—that in which tissue cells which are essential components of the human body take on an entirely new property and become a danger to the body of which they are a part. Doctors distinguish very many different changes of this kind and have many names for the different malignant growths which result, but to the lay public they are all alike and are generally described by the single term of “cancer.” They have one fundamental similarity: they are composed of cells which belong

to one or other of the groups of cells within the body, although their action is far from normal.

It should be made clear at once that all lumps and tumours that develop in or on the human body are not necessarily cancer. The medical man distinguishes between simple tumours, which may grow to quite a large size and may for that very reason produce defects in the organs in which they occur, and those which have malignant qualities and are always dangerous. In the course of the development of the human embryo it occasionally happens that small groups of cells of the one type get misplaced, and as the body grows they come to lie in the wrong part of the body. If these misplaced cells continue to grow they may develop into quite normal tissues reproducing the structure and function, for example, of the gland which they represent. Such collections of cells occasionally lie quite dormant for many years, but they may begin to grow and form recognizable tumours later in life. In the case of such "simple" tumours we are dealing with a quite simple process in which misplaced cells grow and behave quite normally.

In the case of cancer cells we have an entirely different story. One has to imagine a group of cells which are not only misplaced but are capable of growing even more rapidly than the rest of the body cells. More important still, they are capable of spreading, and spreading dangerously, into the tissues and throughout the rest of the body. It is not suggested that all cancers arise in groups of misplaced embryonic cells. On the whole it appears that most cancers arise in tissues which, at least so far as their position in the body is concerned, are perfectly normal. It is the fact that instead of functioning and

growing at the normal rate these cells begin to grow with great rapidity, and they appear to eat into the surrounding tissue—a feature which gives the disease its name, which comes from the latin word for crab (Fig. 15). This process of spreading out into other tissues can actually be seen with the eye in a case of cancer of the skin, but it is the ability to spread into

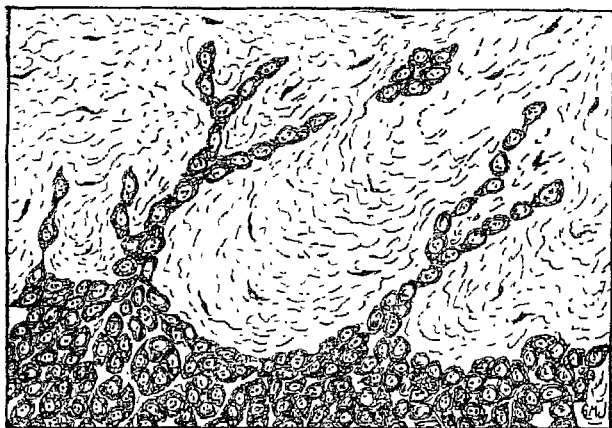


FIG. 15.—A diagram of the growing edge of a cancer; chains and groups of cancer cells are spreading into the surrounding tissue.

more distant parts of the body which demonstrates the terrible nature of this disease. The first stage of growth is usually into the lymphatic glands, which normally carry fluid from the tissues back into the blood stream; from these glands the cancer cells may spread into all the other organs. Some parts, such as the liver, are particularly prone to secondary growths, as they are called.

Cancer cells may destroy the body in which they are growing by invading organs of vital importance. They have, however, a general effect on the whole body. These malignant cells, because of their rapid growth, utilize foodstuffs at such a rate that the rest of the body begins to suffer; loss of weight, and ultimately extreme wasting, are therefore common features of malignant disease.

To sum up, it is clear that in the case of cancer we have a situation in which cells that have arisen from normal cells of the body appear to attack the rest of the tissues. There is evidence that the normal cells put up some resistance to this process and, as a result, some cancers grow very slowly. On the whole, however, the normal tissues are powerless against the malignant cell. The fact that although behaving in this abnormal fashion the cancer cells are very similar to normal cells presents science with an exceedingly difficult problem. For while it is relatively easy to discover methods by which cancer cells may be destroyed, it is exceedingly difficult to find one which will destroy the abnormal cells without at the same time attacking the normal cells of the body.

Up to the present the best weapon against cancerous growths has been to remove them by surgical operation. Many years' experience has shown that if the first group of cells which have become malignant is completely removed by the surgeon, the chances are that the disease will be completely eradicated.

There are two great difficulties. In the first instance, the malignant process may already have gone so far before advice is sought that the surgeon cannot eradicate it. The second difficulty is that while the tumour may be of such a size and in such a situation

that the surgeon can easily remove it, the malignant process may already have reached another part of the body which cannot be dealt with surgically. In spite of these difficulties it is estimated that, among those who are operated upon while the tumour is strictly localized, some 85 per cent. can be described, after five years, as cured. It is necessary to observe such cases over a fairly long period before concluding that the operation has in fact been successful.

In addition to the ordinary methods of surgical removal, radium and certain forms of X-rays are also used in treating cancer. The rays given off by radium have a definite lethal effect on cancer cells. As everyone has become aware since the announcement of the atomic bomb, radioactivity has a deadly effect on many of the cells of the human body. It has been found that in using radium a dose of rays can be given which is just sufficient to destroy the cancer cells without having too serious an effect on the normal cells. The technique is one which requires long experience and careful study, and it may be used by itself or in conjunction with ordinary surgical treatment. One of the fields of research which have been opened up by the atomic bomb is the possibility of developing new methods of splitting the atom that will prove to be of benefit against malignant cells.

It has, in fact, been suggested that we may find a method of curing cancer long before we discover the cause. A great many methods are being tried out. They include not only those of radioactivity, but some in which hormones and hormone-like substances thought to have an effect upon the growth of the body are injected in the hope of interfering with the growth of the cancer cell. Particular success has been ob-

tained in controlling cancer of the prostate gland, and some advance has been recorded in cancer of the breast.

Chemical substances have also been found which definitely interfere in this malignant process. The normal method of division of any living cell is by a process known as mitosis, and in recent years a large number of substances have been found which interfere with the mitotic process. In cancer cells mitosis proceeds rapidly, and chemical substances may be found with the necessary physical properties to interrupt the process of mitotic division and so destroy the cancer cell.

While this research is going on, other scientists are still probing the mystery of the origin of this disease. What is the agent that excites a few cells in the body to take on this alarming propensity? Some believe that the agent must be of the nature of a virus, or of something which, if not closely similar to the virus we recognize in the infections discussed above, is nevertheless akin to it. In support of this idea is the fact that there are certain tumours, particularly occurring in animals other than man, in which the exciting agent can be passed through a filter in the same way as the viruses which we have already described. Such filtered material injected into other normal animals will excite the production of a malignant growth. The stumbling-block is that up to the present it has not been possible to repeat this observation with every type of cancer. Until that is done, it cannot be claimed that a virus is invariably present in these growths.

There are in scientific laboratories quite a number of tumours which can be "transplanted" from one

animal to another and will continue to grow. It is upon these tumours that much of the modern research work is concentrated, for they give such constant results that the effect of various substances upon them can be very quickly ascertained.

One factor that is constantly found in investigations into cancer is that irritation of one kind or another stimulates the activity of cancer cells. We have already mentioned malignant growths which occur in parts of the body where irritation is known to occur. There is the well-recognized chimney-sweep cancer, and there is a definite incidence of cancers among workers handling aniline dyes. There is the well-known case of the Kangri cancer, which occurs in Kashmir. The natives there carry a small bucket of burning charcoal under their clothing to keep warm in the mountains, and sometimes a cancer develops in those parts of the skin with which the Kangri, as it is called, comes in direct contact. There is also the fact that cancer of the tongue is ten times more common in men than in women; in a certain proportion of cases it is quite definitely associated with pipe-smoking.

Experimentally it has been found that, by the application of certain substances isolated from tar to the skin of experimental animals, cancers of certain types can be almost invariably started. This is the best evidence we have that irritation by chemical agents may play a part in the production of malignant growths. There is some evidence that many growths are due to a combination of different factors, but it is possible that the ultimate explanation will be of an entirely novel kind, for this disease is so very different from all the other diseases found in the

human body. Of all the chief killing diseases cancer is perhaps the one which causes the greatest amount of worry in the modern world. This is not surprising when we recall that over 50,000 people in England and Wales die of the disease every year. It is a disease of those over middle age, and one in every seven deaths in people over thirty years of age is due to this condition.

The layman constantly asks if cancer is hereditary, if it is infectious, or if it can be blamed upon any particular mode of living. So far as the evidence goes, the answers to all these points are in the negative. There is no evidence that cancer or the tendency to cancer is hereditary. There are family histories in which it is known that succeeding generations have died from cancer, but when the full statistics are studied it would appear that such cases cannot be regarded as anything more than coincidence.

So with the question of contagion. There are some recorded cases of similar cancers in members of the same family, but the statistical evidence over many years is against the possibility of cancer passing from one person to another.

A great many investigations have been undertaken in an attempt to discover whether cancer is a disease of civilized races. We know fairly well the incidence of cancer in the modern world, but figures for primitive races and other ages are exceedingly difficult to obtain. Allowance has also to be made for a very important factor: in modern times, among civilized nations, the expectation of life is very much longer than in the more primitive races. This means that a larger proportion of people reach the cancer age in civilized communities than among the primitive ones.

On the whole there appears to be no evidence that civilization causes an increased amount of cancer among the healthy. So long as the special predisposing irritative factors we have mentioned are avoided, cancer does not seem to be any more prevalent in one group than in another.

Many people have suggested that particular forms of diet—e.g., the use of fresh meat—and certain methods of cooking, such as the boiling of vegetables, give rise to cancer. Here again statistical surveys of races with different dietetic habits, and also of different sections of our own population, do not support any of these theories. Similarly, no scientific evidence has been produced to show that an existing cancer is in any way affected by a particular form of diet.

Cancer, as we have mentioned, causes more worry to those over middle age than any other disease. The public can assist medical men in dealing with this problem by bearing in mind that every symptom of disease occurring in people over middle age should be properly investigated at the earliest possible moment. People must avoid the tendency to treat what they regard as minor troubles by self-medication or by means of patent and proprietary remedies. These may sometimes relieve symptoms and yet leave the cause entirely untouched and undiscovered.

There is no question that by the proper investigation of minor troubles many cancers would be discovered while still at a stage when the surgeon's knife would ensure complete removal. In so far as fear of operations remains in the population, it must be got rid of, for modern surgery is amazingly safe. While science is striving to forge new weapons against this

disease it is important that we should use, to the best of our ability, those that we already have. With the solution of the cancer problem we shall have approached much closer to the ultimate understanding of the basic physical nature of the living cell; and when that understanding is reached we shall undoubtedly regard the surgical and radioactive weapons of to-day as very primitive indeed. Yet we must remember that they are capable of prolonging and, in a large proportion of cases, of saving life.

CHAPTER XV

BLOOD DISEASES

BLOOD is probably the most astonishing of all the constituents of the body. It not only has its own functions and purposes but also serves as a connecting link between all the different parts of the body. Few people realize that blood as it flows round the body consists of two distinct parts. The first part is fluid, and is purely the vehicle for carrying necessary foodstuffs and chemical products to and from the tissues; and the second, which is carried by the first, is in fact a tissue like all the other tissues of the body. That is to say, it consists of cells that have been specialized for certain duties in the metabolism of the body as a whole.

The chemistry of the fluid part of the blood is a fascinating subject. It reflects whatever is happening in other organs, and its examination constitutes one of the most important branches of modern medical laboratory science. In this chapter, however, it is with the tissue elements of the blood that we are concerned. The blood cells are of more than one kind, and most people are familiar with the fact that they can be divided into the red and white corpuscles. The red cells are present in the body in enormous numbers, many times the number of the white cells, with which we shall deal first (Fig. 16).

There is more than one kind of white cell, and from the way in which their numbers change during the

course of various diseases it appears that each of the types has a special function. As long as health is maintained, the total number of white cells and of each type remains at a fairly constant level. They can be counted by a relatively simple microscopic technique, and they are usually around 7,000 per cubic millimetre of blood. In the diseased body,

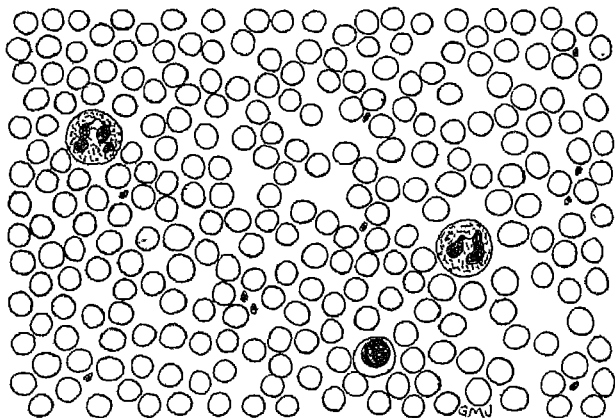


FIG. 16.—Normal blood showing red cells as simple circles, two kinds of white cells, two polymorphs and one lymphocyte, and a few platelets (small solid particles concerned with the clotting of the blood).

however, the number may be greatly altered, either in one direction or the other, and the proportion of the different cells may change over a very wide range.

By far the most common change occurs when there is an acute inflammatory process in any part of the body. In a typical inflammatory condition, such as appendicitis or pneumonia or an abscess, the total number of white cells is increased up to as many as

BLOOD DISEASES

ten times the normal, and the total increase gives some indication of the severity of the inflammatory process. In fevers where the symptoms are obscure, the discovery of this change in the blood is often a valuable aid to diagnosis, since it not only indicates that an inflammatory process is present, but provides in some ways a measure of its intensity (Fig. 17).

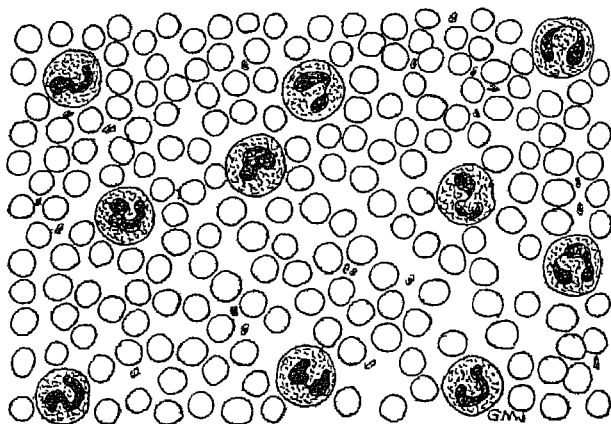


FIG. 17.—To be compared with Fig. 16 to illustrate the increase that may occur in the polymorphonuclear white cells.

The reason for this increase in the total number of white cells is that one class, known as the polymorphonuclear neutrophils, have the function of destroying certain common types of disease germs if they have once entered the body. These white cells are manufactured in the bone-marrow, and as soon as the blood conveys a signal to the bone-marrow that an inflammatory process is going on, large numbers of white cells are produced, pour into the

blood stream, and proceed to the particular tissue which has been invaded by the germ. An abscess—a simple boil, for example—is in fact a collection of these cells, together with the germs which they have attacked and destroyed. In some diseases it is very easy to demonstrate under the microscope how the white cells engulf and destroy the bacteria. In the process many of the white cells are themselves destroyed, but unless the disease is of particular severity the bone-marrow is usually quite capable of sending new ones into the blood stream to make up for the loss. The process by which the polymorphs engulf bacteria is of course precisely the same as that by which amoebae, the most primitive type of animal living in water, digest food particles; and, although these white cells are part of the human body and grow from parent cells in the bone-marrow, they live and act very like the primitive progenitor of the whole animal kingdom (Fig. 4, p. 37).

There are some diseases in which the increase in white cells may be chiefly of the second large group known as the lymphocytes. In normal blood there are usually about one-third as many of these as there are polymorphs (Fig. 16, p. 134). A large increase in the number of lymphocytes may occur in some tubercular infections and also in one or two of the common virus infections. A third type of cell, of which the function is somewhat obscure, is described as the large mononuclear. In glandular fever a marked increase in this type of cell is typical and diagnostic of the disease.

Another frequent change in the blood is caused by parasitic infections. It consists of an increase in the number of the eosinophil cells, so called from their

behaviour when stained with the dye eosin. They are similar in appearance to the polymorphs but take up this particular dye and stain a bright red. Normally they are present in very small numbers. If a parasitic worm enters the body it usually calls forth a sudden increase in the eosinophils, and the discovery of such an increase is always taken as justifying a detailed search for the parasitic invader.

The white cells may, however, also suffer a decrease. This change is found particularly in conditions such as typhoid fever. The blood cells, like all the other tissue cells, are subject to any toxin or poison getting into the blood stream. Some bacterial and other poisons may destroy large numbers and may even prevent their appearance. In the case of typhoid fever we have a relative drop in the number of the polymorphonuclears, so that the lymphocytes appear to be relatively increased.

There are, however, conditions in which the bone-marrow is so badly damaged that it is no longer able to manufacture new cells of the polymorph type and these may practically disappear from the blood stream. The polymorph cells are sometimes spoken of as "granulocytes," because, in addition to a many-lobed nucleus, they contain many fine granules. When they are absent the condition is known by the name of agranulocytosis, and it may be caused by a variety of substances. One of the chief dangers is a chemical called amidopyrine, which is much used as a pain-killer. It was formerly included in certain medicines that could be bought without a doctor's prescription, but when it was definitely proved that its use in susceptible people could produce this damaging effect the drug was brought under the

control of the poisons regulations. This is one of the situations which may occur with new drugs that have not been sufficiently tried out, and it has been noted in connection with quite a large number of substances. Agranulocytosis is one of the delayed-action effects of radioactivity from an atom bomb explosion. It also constitutes one of the reasons why all those working with radium and other materials capable of giving out rays have to be so carefully guarded.

It will be readily understood that such a destruction of the white cells leaves a patient open to the attack of all disease germs with which these cells usually deal. When this condition occurs in the course of an illness the patient usually succumbs to the infection. This possibility has, of course, set the scientist off on a new search, and substances have been found which have the power of stimulating the bone-marrow to produce white cells in large numbers. This is usually done in conjunction with blood transfusion and other measures. Agranulocytosis, however, has not yet been fully conquered.

The changes in the white cells so far described are secondary in nature, being produced by unusual stimuli, mainly those of infections. There are in addition conditions which appear to be primary diseases of the blood cells themselves. These consist of the presence in the blood stream of enormous numbers of one or other of the types of white cell already mentioned. The cells may be increased to such a figure as fifty times normal and, in addition, there appear in the blood stream large numbers of all kinds of abnormal white cells (Fig. 18). The white cell, as has already been explained, arises in the bone-

marrow by development from a more primitive type of cell which does not normally appear in the blood. In the presence of the disease now under discussion, and known as leukaemia, not only are the white cells produced in enormous numbers, but they appear to be produced so rapidly that the more primitive types representing all stages of development are to be found

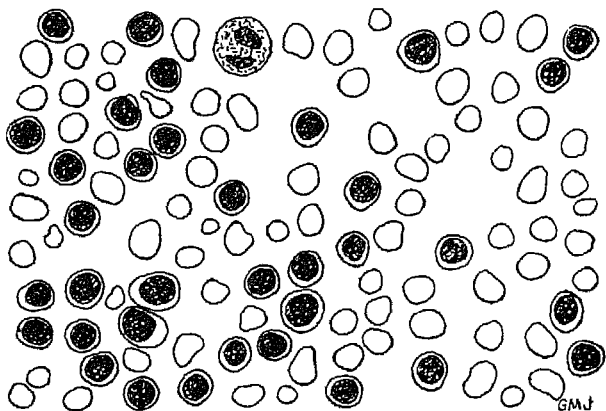


FIG. 18.—The blood in a case of acute Lymphatic Leukaemia in which there is an enormous increase in the number of lymphocytes and, because there is an accompanying anaemia, the red cells are irregular in size and shape.

in the blood itself. The leukaemic process may affect any of the types of normal cells, so that the disease is divided into different types according to the cell affected. The course of the disease, which up to the present has been almost invariably fatal, varies somewhat in the different types.

There is no agreement among medical men as to the cause of leukaemia. For many years the majority

opinion was that this process was similar to cancer in other tissues; in other words, it was thought that the cells behaved exactly as other malignant cells, growing more rapidly, becoming primitive in type, and spreading throughout the body. There are, however, other features of the disease which have inclined some investigators to consider this over-production of white cells as due to an infection by something in the nature of a virus which, interfering with the process of mitosis, sets the cells off on an entirely wrong course of development. Thus it is held that treatment should follow the same lines as the treatment of other virus infections. Up to the present the use of X-rays applied to the spleen, to the bone-marrow, and to the glands, has been the one method that has alleviated the condition and prolonged life. In very recent times other substances have been discovered which definitely interfere with mitosis and are capable of producing very marked reductions in the number of leukaemic cells. This work awaits a final opinion, but it opens up an entirely new line of attack on a disease which has up to the present been one of the most disheartening with which medical men have had to deal.

The red cells are really a tissue entirely separate from the white corpuscles. They have the most important functions of carrying oxygen from the lungs to all the tissues of the body and of returning with carbon dioxide, which is a waste product of tissue metabolism and is exhaled in the breath. The red cells carry out this unction by virtue of containing a remarkable substance, haemoglobin, which can rapidly take up oxygen from the air breathed into the lungs and yet will hand it on with equal facility to any tissue in the body which requires it. The

amount of haemoglobin present in the blood in normal health is another of those things which remain remarkably constant; but haemoglobin is also one of the substances most affected by disease, and any diminution in its amount interferes with the oxygen-carrying capacity of the red blood cells. The red cells are small disc-like objects, and there are 5 million of them in a cubic millimetre of blood (Fig. 16). The total number present in the body is many many millions, and all of them are manufactured in the bone-marrow. They differ from all other cells in the body in that they have no nucleus, but they are in other respects composed of living protoplasm and their life is limited. The bodies of those that die, and the precious haemoglobin that they contain, are dealt with by the spleen and the liver so that the necessary oxygen-carrying material may be conserved in the body.

The red cells are also subject to detrimental influences, and anything of a poisonous nature which reaches the blood stream may affect them. In most diseases caused by a germ there is usually some poison or toxin circulating in the blood from the germ, and the red cells may be damaged by it. When this occurs the number of red cells falls and the patient becomes anaemic. The number of cells, however, may by an effort of the bone-marrow be kept up to fairly normal numbers, but each cell may contain less than its normal amount of haemoglobin. In either case we have what is called a secondary anaemia, which can usually be cured by the removal of the toxic agent and by giving to the patient an amount of iron large enough to make up for the destruction of haemoglobin.

Like the white cells, the red cells may also suffer from diseases which affect them primarily. One or two are rather strange and somewhat rare conditions, but they merit a brief mention. There is, for example, "sickle cell anaemia," in which the normal disc shape of the red cells is entirely lost and all kinds of abnormal shapes occur, the chief one being that of a sickle. This strange disease is apparently confined to those with negro blood. There is in this and in all other countries another disease, which is familial, in which the red cells appear to be more spherical than normal, and also more fragile and therefore more liable to be broken down by noxious influences. Beyond the fact of its occurrence in families, this disease—acholuric jaundice, as it is called—remains something of a mystery, but it is successfully treated by the removal of the spleen.

The most important of the primary diseases of the red cell is that known as pernicious anaemia, which at one time was invariably fatal. It is not particularly common, although before present methods of treatment were discovered it caused the death of a few hundred people each year in this country. It was first definitely recognized about 100 years ago and, because of its very definite diagnostic features, has always attracted much medical attention.

In pernicious anaemia there is a steady decrease in the number of red cells; the patient begins to appear a little yellow in colour, and slowly loses strength. Very often the tongue becomes sore, but at first the patient is not alarmed because the process is usually very slow and gradual. At a later stage certain symptoms, which are due to changes in the nerves, begin to appear and difficulty is found in

walking. At this stage the blood will present a picture which is easily recognized (Fig. 19). There is, of course, a severe anaemia with probably only between 20 per cent. and 30 per cent. of the normal haemoglobin. In the more common secondary anaemia the amount of haemoglobin in each red cell is below the average, but in pernicious anaemia the

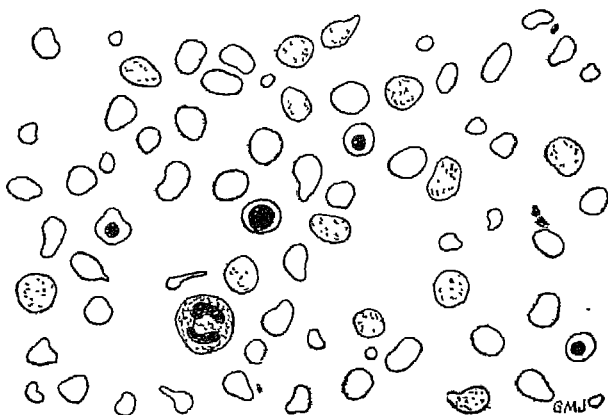


FIG. 19.—The blood in pernicious anaemia early in treatment. The cells showing small dots are the new red cells, or reticulocytes. Three red cells containing a nucleus are also shown.

reverse is found, and the average cell is larger and contains more than the normal amount of haemoglobin. The cells, however, are of all shapes and sizes, and there may be primitive forms present. When careful measurements are made the average size of the cells is found to be greater than normal, and this is always the final diagnostic point.

It will be seen from this that the condition of the

red cells is due, not to lack of haemoglobin, but to the inability of the bone-marrow to produce new normal cells. In its attempt to do so it produces the abnormal forms that are found in the blood stream, including some with a nucleus. It is a disease which may show natural remissions, but it was only in recent years that some idea of its cause and, of possible methods of treatment was obtained.

From this work it appears that the normal production of red cells is another part of the human mechanism which depends on a delicately adjusted balance between substances present in the food we eat and substances stored by one of the glands of the body—namely, the liver. So long as both these factors are present we can go on manufacturing normal numbers of normal red cells. In pernicious anaemia patients the factor stored by the liver and elaborated by glands in the wall of the stomach is missing. All animals have the same mechanism, and it has been found that the liver of animals normally contains large amounts of this vital substance, which can be extracted and can be administered to human patients either by mouth or by injections. To-day we have available liver extracts of great purity and very high quality, and the average case of pernicious anaemia can be treated and kept well by injections of these extracts. It is of course vital that patients should continue with this treatment for the whole of their life, but to-day this usually means no more than one injection a month to keep the blood at a perfectly normal level. There is, however, no method by which the potency can be tested except on a patient suffering from the disease. Up to the present the one reliable test is to discover what any particular extract can do

to relieve the sufferer from the disease. When a potent extract is injected into such a patient by the usual intra-muscular method, the change that takes place can be followed in the red blood cells themselves. It is usual to select a patient whose blood contains about 20 per cent. of the normal number of red cells for the test. By a special method of staining, new red cells can be distinguished from old ones. These new cells are called "reticulocytes," because with this staining method a fine dark reticulum, or network, is seen within the body of the new cell. Pernicious anaemia patients, before treatment, show practically none of these cells in the blood. Within a few days of the injection of a potent liver extract, large numbers appear, and figures as high as 40 per cent. of new red cells have been obtained (Fig. 19, p. 143). All the cells rapidly become normal in size and shape, losing the potentiality of breaking up and disappearing from the blood. In a few weeks figures will be obtained that are practically normal.

So long as the patient receives a sufficient amount of such liver extracts, the blood will behave exactly like that of a normal person. Pernicious anaemia is very largely a disease that occurs after middle age, and it is astonishing to see the way in which the blood responds to adequate treatment even in the aged. It should be emphasized that pernicious anaemia requires careful examination of the blood, and doubtful cases may require repeated counts of the blood cells, together with other tests, in order to establish the diagnosis. In some cases it is necessary to examine the bone-marrow itself. This is done by pushing a needle through the outer layer of the breast bone and sucking a small amount of bone-marrow from inside by means

of a syringe, and making the necessary smears of that marrow for examination under the microscope. Good preparations enable the expert to tell exactly what is happening to the production of the new cells, and as there are rare cases simulating pernicious anaemia but not responding to liver extract treatment, such examinations have to be carried out to make the diagnosis absolutely certain. As treatment goes on it is essential that the blood should be controlled by periodic examinations. In the past there have been considerable difficulties about this, both because laboratory services have not been fully developed and because National Health Insurance did not cover the cost of such examinations. In the new National Health Service it is promised that all such investigations will be available to every citizen, and when that is realized the control of pernicious anaemia will be complete.

In concluding this chapter we should refer again to the fact that, in order to keep up the supply of new red cells, the bone-marrow not only requires the stimulus that comes from the liver factor which we have just seen to be essential in pernicious anaemia, but also a constant supply of iron for the manufacture of haemoglobin. The liver and spleen endeavour to save the haemoglobin from those red cells that have completed their work, but there is always a loss apart from the losses due to disease, and this must be replaced. Iron is present in most diets, but unless a sufficient amount is available the normal haemoglobin level cannot be maintained. It has been found that a "nutritional" anaemia may occur not only in young babies but also in adults. Investigations have shown that this is particularly common among

working-class mothers, especially those who have many children, and that it is entirely due to the economic condition of these women and can be prevented by the simple device of giving iron by the mouth. This is a type of comment on our present economic arrangements which medicine in its social aspect is being forced to make more and more often. The maintenance of a normal blood supply, and with it the maintenance of a perfect and healthy body, are so closely bound with the conditions under which the human being lives that until we can be sure that all the essential ingredients in diet and in environmental conditions are available for everybody, we cannot expect to have the healthy race that has been made possible by the many marvels within the human body and by the progress of science.

CHAPTER XVI

THE FUTURE

So far we have discussed medical science and the problems that face it as though the whole of the subject could be covered by an investigation into the causes and effects of disease and into methods of treatment and ways in which the patient can be cured. To a much smaller extent we have discussed the prevention of disease by interfering with those agents which attack the human body from without. Health, however, means much more than that; it means much more than the mere absence of disease, for the truly healthy person is one that is not only free from disease but who is able at the same time to enjoy life to the full and to carry out with vigour and initiative all that is asked of him in the environment in which he finds himself. The preservation of that degree of health is something in which the individual must play his or her part; but protection of health has become one of the primary duties of the State, because it is the action which the State takes in relation to the whole economic and social structure that determines the environment to which the individual must be adapted.

To-day we witness a new effort on the part of the State to improve the environment and to provide a better health service. With this health service we are entering a new era, in which the State assumes full responsibility for the health of the community as a

whole and of the individual, but in which the individual is expected to make the efficient running of that system one of his main concerns. Consequently the individual may demand that the State should do much more than it has done in the past to provide a suitable environment. When the State first turned to this aspect of health, it sought to prevent disease by ensuring an adequate system of sanitation in all our large cities. So far as rural areas are concerned sanitation has still to be provided, and for a great number of people a good supply of safe drinking-water in the home has still to be made available.

The most important problem still to be brought to a satisfactory position is that of housing. It is now generally accepted that it is the duty of the Government to approach this problem with due regard for the health of the individual citizen. Health of the kind we are discussing is not possible so long as people are compelled to live in overcrowded, insanitary, and unclean houses. Overcrowding will undoubtedly be dealt with very rapidly by the plans now being pursued, but a great re-housing of the people of this country will still be required. To the mother and children the environment provided by the home is particularly important, and we cannot consider the health aspects of housing to be solved until everyone has a house in which there is ample accommodation for the whole family, in which the possibilities of disease and accidents are reduced to a minimum, and which is placed in the kind of surroundings which will give the necessary air and light, and which will have all the other amenities that are now recognized as necessary for citizens in a modern State.

In addition to the whole environment the worker

has to be protected by better and fuller laws in regard to industrial hazards and factory conditions. In this field, during the present century, there has been a considerable advance, but much more remains to be done. Two things are vital in the immediate future. On the one hand we must have a system whereby all young people entering industry, and all people working in industries to which any known or any probable hazards applies, will have periodic health examinations, with a guarantee that the worker will be provided with any medical care found to be necessary, and that his or her financial position will be made as secure as possible. On the other hand, we must as quickly as possible provide a complete industrial health service covering all aspects of health in factory, workshop, and office, and closely linked with the home health system.

We have also to improve the dietary condition of the people of every country. It is generally accepted in medical circles that, in spite of certain deficiencies, war-time dieting, coupled with the policy of fixing the prices of essential foodstuffs, has resulted in a better nutritional state for the nation as a whole. Before the second World War quite a large proportion of the population of these islands were on or below the level of diet at which a bare minimum of good health can be maintained. Abounding health is possible only when the food eaten is varied, contains certain essential ingredients, and supplies all the different components of a perfect diet which are well known to medical science. This, of course, is not a problem for the people of Britain alone. Our food comes from many countries and our dietary needs are bound to the dietary needs of all people and to the general economic

system. Rationing and fixed prices have shown that a minimum diet which will sustain health can be placed within the reach of all by suitable planning. The health of the future depends upon some international method of guaranteeing an adequate diet to all.

This is an age of new discoveries and of great advances. The proof of the germ theory of disease opened up many new paths to the control of disease, and one of these was aimed at preventing diseases from entering one country from another. This led to two things, the first being the establishment of quarantine laws by which sufferers from certain diseases could be prevented from entering a country. Because of the long delay at ports and frontiers which they caused, they were modified or replaced by other laws, under which only those who could be suspected of being potential carriers of particular diseases were prevented from entering one country from another immediately. These laws have been effective, but to-day we are threatened with new difficulties. When communication between one country and another was slow, there was time—for example on long voyages—for diseases that had been acquired at one port, but had not yet completed their incubation period, to reveal themselves. With modern air transport this does not happen, and special steps have to be taken, not only to see that those using air transport are not carrying disease, but that the aeroplanes do not carry any of the vectors, such as mosquitoes, which might spread some of the diseases we have described in these pages. The spraying of aeroplanes with substances such as D.D.T., which destroys insects, is of course now a routine procedure.

The other matter that arose from the recognition that disease could and did disregard national boundaries was the building up of the practice of exchanging medical knowledge and news of new discoveries between the medical men of one country and another. In addition to that, the League of Nations built up a health organization with the definite intention of standardizing medical procedures throughout the world, and agreements have been reached in many fields. In those diseases which can be treated by sera there is an international agreement as to the way in which the sera shall be used and how the dosage will be standardized, so that all doctors in all countries use the same procedure for treating a case.

To-day the rate of advance in medical science has been speeded up enormously. So, too, has the quality of the discoveries, for not even the greatest advances of Pasteur, Lister, and other great men have excelled the discovery first of all of the sulphonamides, and later of Penicillin. To the latter, war gave a great impetus, so that, in spite of the difficulties of producing it by mass-production methods, great amounts were made available for Allied troops, and now for the civilian population of the whole world. Penicillin is, however, not the final word, for many diseases are beyond its power. New discoveries of a similar nature are being tested out, and throughout the research laboratories of the entire world there is a tremendous air of expectation. Whether one method of treating all bacterial and virus diseases will be discovered is doubtful, but we already have weapons that deal with a large number of them. Cancer is not yet conquered, but the physicists who are engaged on the splitting of the atom are forging new weapons

that may be used against that disease. The chemist has also made advances, and there is now a race between the research workers in different fields to see who will be the first to solve these mysteries.

The present and the future are not, however, without their danger. There is evidence that some of the bacterial diseases, and possibly some of the virus diseases, which we now recognize have not always existed. Early descriptions of disease were of course far from scientific, and it may be that if they were accurate we should at least know that from the time man began to leave historical records there has been no new disease. Many investigators, however, believe that there have been, if not new diseases, at least great changes in the virulence of certain germs; and it is always possible that one of them might at some future date acquire a greater ability to attack the human body and prove, therefore, much more dangerous than at present. In our modern methods of treatment there is also a danger. Germs can learn how not to be killed by certain drugs, and this has been very speedily shown in connection with the sulpha drugs. These sulpha drugs have proved an enormous boon in dealing with such germs as the haemolytic streptococcus and the gonococcus. If given in adequate dosage they can clear the body of these germs very quickly. If, however, the dosage is inadequate some of the germs may become resistant to the drugs—may acquire the ability to go on growing in spite of the presence of the drugs. The discovery of Penicillin has removed some part of the danger, for strains of those germs that have become resistant to the sulpha drugs are usually still susceptible to Penicillin; but many bacteriologists are afraid to think what our

position would be if strains of germs should arise which are resistant to sulpha drugs and Penicillin. So far, the danger is negligible, but it is mentioned to illustrate that medical science can never be content with one discovery, with one method of treating a disease, but has always to be looking for better ways of protecting the human tissues.

This and many other factors impress us with the fact that prevention must be the keynote of medical science in the future. Many methods will have to be employed: those that immunize the individual against a particular disease; those that deal with the insect or other carrier of the disease; and those that deal with the environment as a whole, so as to remove the sort of conditions which bacterial agents like. It has been suggested, also, that at some still distant date the science of genetics, yet in its infancy, may enable us in some way to modify the human race so that we may eliminate certain mental and physical defects which we know to be hereditary, and even that we may be able to build up a stock which is more resistant to disease.

Greater even than the prevention of disease will be the promotion of health. Those who manage to escape infections must be put in a position to enjoy physical fitness to the greatest extent and to make the greatest possible contribution to the work of the community. Co-operation between the public and medical scientists will be essential; and that co-operation implies a knowledge of the whole subject which up to the present has been possessed by too few. The education of the general public on matters of health will undoubtedly be a great feature of the future health service. Propaganda may be general,

telling something of the story of health and giving simple rules for its preservation; or it may be particular, aiming at the abolition of habits considered to be wrong or at a particular disease which is prevalent in the community at any given time. The setting up of health centres, which are to be built by the major local authorities of this country, will provide us with a place at which the education of the public in health can take place. It will have to be done with great care; we must not risk the danger of making people afraid of disease without giving them a more positive attitude towards health. The film, the lecture, the discussion group, and all other modern techniques will require to be used, and ultimately it is hoped that the people will learn to present themselves for regular health examinations. The records of these examinations will be kept for future reference, and gradually a nation as much more healthy than the present generation as that generation is healthier than its predecessors of 100 years ago, will develop in this country.

In the new medical organization every doctor has the opportunity of making his contribution to the prevention of disease. When the service is fully operative, medical men should have the leisure that is necessary for study and should be able to keep abreast of all new developments. All doctors should also be enabled to play their part in investigating the problems that are still unsolved, and 'by the perfect relationship between them and their patients which the new service makes possible should be able to obtain the help of the public in any investigation that is taking place.

Those developments will be reflecting changes that

are taking place in the medical organization of every country in the world, and the field of medical science is one in which full co-operation between nations should be realized at a very early date. The problem of our time is to obtain co-operation among all nations in all fields, and since the aims of medicine are identical in all countries there should be no bar to the setting up of international methods by which all doctors co-operate, not only to solve the remaining problems of medicine, but also to protect, to preserve, and to promote the health of the citizens of the world.

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